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## CONTENTS OF PREVIOUS NUMBER

JULY, 1926. NUMBER 7


Hereditary Hemorrhagic Telangiectasia. Charles Mallory Williams, M.D., New York.

Significance of Cutaneous Stimuli for Protection of the Body Against Infection. Alois M. Monnheimer, M.D., Cincinnati.

Infantile Acne Vulgaris: A Report of Three Cases. Samuel Ayres, Jr., M.D., Los Angeles.

Granuloma Inguinale: Clinical Observations, Vaccine Treatment and Allergic Reactions. Max Goldsieker, M.D., and Samuel M. Peck, M.D., New York.

Lymphosarcoma: Report of Two Cases. Frank C. Combes, Jr., M.D., New York.

Fordyce's Condition of the Penis: Report of a Case. William H. Goeckerman, M.D., Rochester, Minn.

Schamberg's "Peculiar Progressive Pigmentary Disease of the Skin." Lawrence E. McCafferty, M.D., New York.

Lymphogranulomatosis Inguinalis. V. Pardo-Castello, M.D., Havana, Cuba.

The Fox-Fordyce Syndrome. Herman Goodman, B.S., M.D., New York.

Clinical Notes:

Trichotillomania. L. G. Feinhauer, M.D., Pittsburgh.

News and Comment.

Abstracts from Current Literature.

Society Proceedings:

Chicago Dermatological Society.
New York Academy of Medicine, Section on Dermatology and Syphilis.
Philadelphia Dermatological Society.
Pittsburgh Dermatological Society.
New York Dermatological Society.

Book Reviews.

Index to Current Literature.


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Archives of Dermatology and Syphilology

VOLUME 14 AUGUST, 1926 NUMBER 2

# A STUDY OF THIRTY-FOUR CASES OF RAPIDLY DEVELOPING SYPHILITIC PARAPLEGIA *

MON-FAH CHUNG, M.D.
Assistant Neurologist, Peking Union Medical College
PEKING, CHINA

A rapidly developing syphilitic paraplegia is by no means a rare neurologic occurrence in China. Indeed, the frequency with which one encounters the disease here and its apparent rarity in the experience of certain writers in foreign countries, deserves attention. In a review of the literature, Cole [1] reported two cases of acute syphilitic transverse myelitis and concluded that this condition was rare, although he was of the opinion that "it is a disease much commoner than the literature would lead us to believe." Nonne,[2] while stating that "acute tranverse myelitis is not an infrequent form of spinal syphilis," found a total of only eight cases (3.8 per cent) of the 212 private and hospital patients under his care. Williamson [3] in his list of spinal syphilis (excluding tabes) mentioned six of thirty-five cases or 17 per cent, but Orlowsky [4] recorded nineteen of his seventy-two cases of spinal syphilis or 26.4 per cent. These percentages fall far below that which Spiller [5] quoted in 1895 in a conversation with Dejerine, namely, 40 per cent of all cases of spinal syphilis. It might therefore be of particular interest to note how close to the latter's estimation our figures here approach.

Various observers in different parts of China, as Woods [6] in Canton,

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* From the Department of Neurology of the Peking Union Medical College, Peking, China.

1. Cole, H. H.: Acute Syphilitic Transverse Myelitis, Arch. Dermat. & Syph. **9**:102-113, 1924.

2. Nonne, Max: Syphilis und Nervensystem, 1921.

3. Williamson, R. T.: Diseases of the Spinal Cord, Oxford Med. Pub., 1908.

4. Orlowsky, quoted by Mott, F. W., in Syphilis of the Nervous System, in A System of Syphilis, edited by Power and Murphy, 1910.

5. Spiller, W. G.: Sudden Paraplegia, Arch. Neurol. & Psychiat. **13**:471, 1925.

6. Woods, A. H.: Diseases of the Spinal Cord Among the Chinese, China M. J. **32**, March, 1918.

Maxwell [7] in Shanghai, Hodge [8] in Hankow, and Lennox [9] in Peking, are all in accord as to the common occurrence of this type of spinal paralysis. No less than twenty-five cases of paraplegia, the majority of which are syphilitic in origin, have come under our observation annually. Adopting Williamson's classification of syphilitic spinal diseases, we have arranged the cases admitted to this hospital for the past eight years as follows:

| | |
|---|---|
| Chronic syphilitic disease of vertebrae | 1 |
| Meningomyelitis | 10 |
| "Acute" paraplegia | 34 |
| Chronic spinal paralysis—"Erb's" | 16 |
| Chronic transverse myelitis | 23 |
| Gumma of the cord (verified) | 1 |
| Tetraplegia | 2 |
| | 87 |

From this distribution, it will be noted that the incidence of "acute" syphilitic paraplegia reaches 39 per cent of all spinal cases, a figure from which we may safely infer that this form of nervous infection is prevalent in China.

### TYPES ACCORDING TO SYMPTOMS

In studying our cases, we are able to distinguish clinically three types, namely: (1) a form with either a complete loss or a reduction of all sensations and a complete motor paralysis; (2) one with a dissociated sensory disturbance and paraplegia; and (3) one with no sensory involvement and only the motor function affected. These groups may be illustrated by the following cases:

CASE 1.—A coolie, aged 44, was brought to the hospital on March 14, 1919, with a complete paralysis of both lower extremities, which developed within twenty-four hours, beginning with pain in the abdomen, a sense of tightness around the waist, vomiting, numbness and weakness of the legs, and difficulty with urination. He admitted a primary sore a year before. On examination, sensation was found absent from the waist down with loss of motor power and of all reflexes, and no Babinski sign or clonus. The sphincters were spastic and bedsores were present on the buttocks. Wassermann tests of the blood and spinal fluid were strongly positive. An intensive course of arsphenamine was given with but slight improvement in his condition when he was discharged three weeks later. He was readmitted a month after discharge with no movements of the legs but with return of sensation, increased deep reflexes, bilateral Babinski sign and ankle clonus, incontinence of urine and feces. Another course of treatment was administered. The patient left the hospital the second time eleven weeks after entry with slight return of muscular power of the legs. Wassermann tests of the blood and spinal fluid at that time were negative.

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7. Maxwell, James: Syphilis Among the Chinese, China M. J. **27**:379-386 (Nov.) 1913.

8. Hodge, S. R.: Syphilis in China, China M. J. **21**:237-241 (Sept.) 1907.

9. Lennox, W. G.: Neurosyphilis Among Chinese, Arch. Neurol. & Psychiat. **9**:26-33 (Jan.) 1923.

CASE 2.—A student, aged 22, was admitted on Feb. 20, 1925, for paralysis of both legs and retention of urine, which came on seven days before entry, when on awakening he found himself helpless. He confessed having had a chancre four years before onset. Examination revealed a loss of only the temperature and pain sensations from a level just below the umbilicus (eleventh thoracic segment) to the toes, with touch, vibratory, joint and muscle sensations undisturbed; abdominal and cremasteric reflexes were present, but knee and Achilles' reflexes were absent. There was no Babinski sign or clonus; the sphincters were spastic; there were bedsores on the buttocks and cyanosis and dryness of the skin of both lower legs and feet. The blood and spinal fluid Wassermann tests were strongly positive, with a cell count in the latter of 38, protein, 0.84 mg. per one cubic centimeter and a colloidal gold curve of 1123211000. Antisyphilitic treatment was immediately instituted. Improvement was noted three days after entry. The sensation of the legs returned gradually and was complete within a month; motor power also slowly reappeared with beginning increased reflexes, Babinski sign and clonus; the bedsores healed, and there was some return of voluntary sphincter control. The patient was discharged three and a half months after entry, able to walk about with support.

CASE 3.—A monk, aged 24, came to the outpatient department in a wheelchair on Sept. 4, 1924, complaining of inability to pass urine, to stand or walk. His illness commenced eight days before admission, with weakness and numbness of both legs, followed by difficulty with urination three days later, and by paraplegia on the morning of the visit. He denied having a chancre, but admitted a Neisserian infection. Examination showed no objective sensory disturbance and practically a complete motor paralysis; abdominal reflexes were absent but the cremasteric reflexes were very weak; patellar and Achilles' reflexes were exaggerated, with a bilateral Babinski sign and ankle clonus; the sphincters were spastic and sexual desire below normal. There was no evidence of recent infection, tumor, tuberculosis or trauma. The blood Wassermann test was strongly positive. The patient was to have returned for further study, but never reappeared at our clinics.

Cases listed under group 1 are clear-cut transverse lesions, and vary only in the degree of the injury which affects the components of the cord. Group 3, except for the nature of the onset, resembles closely the class of cases which was first described by Erb[10] in 1892. We presume that with the progress of time, when the early acute symptoms have been forgotten by the patients, such cases might be erroneously regarded in the category of "Erb's paralysis." Group 2 is particularly interesting not only in that the sensory dissociation is not unlike that which characterizes syringomyelia, but in the probable pathologic basis of the lesion, for Spiller[11] in 1909 recorded such a case of sudden paraplegia with partial loss of only the pain and temperature sensations, and confirmed by microscopic evidences a degenerative process involving the anterolateral portion of a few segments of the cord, which resulted from a thrombosis of the anterior median spinal artery.

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10. Erb, W.: Ueber Syphilitische Spinal-Paralyse, Neurol. Centralbl., 1892.

11. Spiller, W. G.: Thrombosis of the Cervical Anterior Median Spinal Artery, J. Nerv. & Ment. Dis. **36**:601-613, 1909.

PATHOLOGIC ANATOMY

I agree with Buzzard and Greenfield [12] that the "syphilitic changes in the bloodvessels and meninges" spread "over a much wider area of the cord than the clinical symptoms have suggested," and also with their point of view that "it is probably often the case that the latter (clinical symptoms) have been determined by an *acute* or *subacute* interference with the circulation brought about by vascular thrombosis of one or more important vessels." I would go further than they in stating that only in the cases of sudden paraplegia, which develop with little or no premonition, the meningitic process, although widespread, is not prominent and that the thrombotic lesions are confined to "one or more important vessels," but that in the cases of "subacute interference" with the blood supply, when the clinical symptoms develop less rapidly and extend over a longer period, say a month or less, the changes in the meninges and blood vessels correspond to those of a severe meningitis. It is in these subacute cases that a rich exudate of cells, chiefly lymphocytes, plasma and endothelial cells, is found in the meninges, as well as an extensive infiltration of round cells in and about the walls of the blood vessels, marked peri-arteritis and endo-arteritis and phlebitis, gradually impinging on the circulation of the smaller vessels about the periphery of the cord, and consequently interfering with its nourishment. The retrograde changes in the cord itself, consisting of softening and disintegration of neural elements at the site of the lesion, and ascending and descending degeneration of the tracts with chromatolysis of the ganglion cells in the gray matter above and below the lesion, are largely, if not entirely, secondary to such interference with the blood supply.

On the other hand, in contradistinction to the foregoing picture, I have recently described pathologic findings in two cases of sudden syphilitic paraplegia, in which I found only thrombosis of the spinal vessels—in one, of the dorsal group of arteries, and in the other, of the veins about the cord—with little or no infiltration of cellular elements in the blood vessels or meninges, indeed, hardly any evidence of a meningitis. Secondary myelomalacia and other changes of a transverse cord lesion had resulted in both cases. Only on the basis of vascular lesions not unlike that of a cerebral apoplexy from thrombosis can the acuteness of the onset be explained. A hematomyelia or an intramedullary thrombosis or even an embolus may give rise to similar symptoms, but lesions of this nature are as rare in the cord as thrombosis or hemorrhage is common in the cerebrum.

Recognition of the rôle played by vascular thrombosis in the production of rapid paraplegia, especially in syphilis, in which the vessels are

12. Buzzard, E. F., and Greenfield, J. G.: Pathology of the Nervous System, 1922, p. 142.

so frequently attacked in the early stages of the disease, is by no means recent. Spiller [11] and Bastian,[13] both in 1909, had pointed out the importance of these circulatory lesions. Just as the spirochetes invade the blood vessels elsewhere in the body during the course of the infection, so are they likely to attack the vascular elements in the nervous system, producing changes which lead to the narrowing or obliteration of the lumina of the vessels, thereby causing a diminution or complete stoppage of the blood supply to the nervous tissue, which, more than other tissues of the body, suffers readily from the lack of proper nourishment.

## ETIOLOGY

The direct cause of the paraplegia in all of our cases is syphilis. Twenty-two of the thirty-four cases gave not only a history of syphilitic infection, but also showed penile scars and positive Wassermann reactions in either the blood or the spinal fluid or in both; six denied any primary sore, but the serologic findings were conclusive; and the remaining patients admitted a primary lesion with negative laboratory data. Cases with suspicious history of syphilis but without either physical evidences or laboratory confirmation, have been excluded from this report. Among the precipitating factors, we can name exposure to cold, exhaustion, overstrain, trauma, upper respiratory infections and dysentery as being among the more frequent accompaniments at the time of the onset. Other factors such as sexual excess and alcoholism have been mentioned by various writers.

Occupation seems to play no part, although the majority of our cases are confined to the soldier and coolie classes.

With regard to sex, all of our cases were found in males. Practically all the data in the literature concede the preponderance of this type of syphilitic disease among the masculine element. We must, however, state that syphilitic paraplegia is rare among Chinese women, but presume that it does occur among them, for we have seen cases of chronic myelitis in our clinics.

In the matter of age, eighteen of our cases occurred in the third decade, seven in the second, seven in the fourth and two in the fifth. This corresponds with the records of the cases reported in foreign literature, most of which fall within the second and third decades.

*Interval Between Primary Lesion and Paraplegia.*—Cole [1] calls attention to some interesting figures with reference to the duration of syphilis in relation to myelitis. He discovers in his own two cases and from his review of the reported cases that a large number of them "appeared within from fifteen to eighteen months after the beginning

13. Bastian, H. C.: Thrombotic Softening of the Spinal Cord as a Cause of So-Called Acute Myelitis, Lancet **2**:1531, 1910.

of syphilis." Our cases run parallel with his findings, as thirteen of our series fall within the period from six to eighteen months, ten between two to four years, and four between five and ten years. The average interval between the primary sore and the onset of paraplegia of all our cases is two and four-tenths years, our earliest case being six months after the initial lesion, the latest, ten years and the largest number occurring during the first year.

### SYMPTOMATOLOGY

From the nature of the onset, two distinct divisions can be made out, namely, the acute and subacute groups of syphilitic paraplegia. The acute forms comprise those in which the paraplegia occurred over night or within from twenty-four to forty-eight hours, preceded by little or no prodromal symptoms, and resulting in a complete flaccid paralysis of both lower limbs, invariably with sensory disturbances, loss of sphincter control and trophic changes; while the subacute type includes those with premonitory symptoms extending over a period of a few days to three weeks and with either a flaccid or a spastic paralysis, some sensory fault, sphincter trouble, and trophic changes. This three week limit is taken because in our experience it was based on our observation of the chronic spinal cases; when total paralysis did not occur within this time, its development as a rule extended over a much longer period. According to the table, it will be noted that eight cases come under the acute type, and the remaining twenty-six under the subacute heading.

In the acute cases, the paraplegia and bladder symptoms were simultaneous, although the former might precede the latter or vice versa within a relatively short time; in the subacute types, the development of the symptoms varied. Sixteen commenced with numbness of the lower extremities, five with difficulty in urination or retention, four with weakness of the legs or difficulty in walking, and only two with pains in the back. Pains in the back are reported in foreign literature as being a frequent prodromal complaint. As a rule, the bladder and rectal symptoms antedated the paralysis, but we have ten cases in which the reverse was found to be true. Probably in these acute cases, they were usually coincident. Numbness was not present in all of our cases, but bladder symptoms, either difficulty with micturition or retention, less frequently incontinence, were invariably associated with the lesions.

The sensory manifestations varied considerably. Thirteen of our cases showed a complete loss of all forms of sensation below the lesions; eleven, a varying degree of hypesthesia for all forms; four, only thermoanesthesia and analgesia; and six, no objective changes. Practically in every case subjective paresthesia was present. The sensory findings apparently depend on the degree of stoppage and the particular areas

*Observations in Thirty-Four Cases of Syphilitic Paraplegia.*

| Age | Sex | Duration Since Primary Infection | Period of Onset to Paraplegia | Prodromal Symptoms | Lower Limbs | | | Sphincters | Wassermann Test | | Spinal Fluid Cells | Condition at Discharge |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Sensation | Motor | Deep Reflexes | | Blood | Spinal Fluid | | |
| 22 | M | Denied | 3 wks. | Numbness; difficult urination; paralysis..... | Absent | Lost | Feeble or absent | Lost | ++++ | +++ | 90 | Died |
| 35 | M | 7 yrs. | 24 hrs. | Weakness; sphincter trouble; paralysis..... | Absent | Lost | Left, lost; right, absent | Lost | ++++ | ++++ | 12 | Died |
| 31 | M | 1½ yrs. | 11 days | Numbness; difficult urination; weakness..... | Absent | Lost | Absent | Lost | ++++ | ++++ | 13 | Improved |
| 31 | M | 4 yrs. | 10 days | Numbness; difficult urination; weakness..... | Diminished | Lost | Increased | Lost | ++++ | +++ | 4 | Improved |
| 22 | M | 4 yrs. | Over night | Paralysis; retention of urine and numbness.. | Temp. and pain, 0; touch and vibratory sensation, P | Lost | Absent | Spastic | ++++ | +++ | 38 | Improved |
| 44 | M | 3 yrs. | 3 days | Numbness; difficult walking and urination.... | Absent | Lost | Absent | Lost | ++++ | Neg. | 10 | Unimproved |
| 27 | M | 1 yr. | 7 days | Numbness; paralysis; retention..... | Absent | Lost | Absent | Spastic | ? | ? | ? | Slightly improved |
| 35 | M | 5 yrs. | 24 hrs. | Sudden paralysis with incontinence..... | Absent | Lost | Absent | Lost | ++++ | + | 30 | Died |
| 35 | M | 6 mos. | 8 days | Numbness; retention; weakness of legs..... | Absent | Lost | Absent | Lost | ++++ | ++++ | 900 | Improved |
| 44 | M | 1 yr. | 24 hrs. | Sudden paralysis with retention..... | Absent | Lost | Absent | Spastic | ++++ | ++++ | 400 | Improved |
| 50 | M | 10 yrs. | 3 wks. | Difficult urination; numbness; paralysis..... | Touch, P; pain, 0 | Lost | Absent | Lost | ++ | ++++ | 9 | Unimproved |
| 33 | M | 1 yr. | 2 days | Retention of urine; numbness; paralysis..... | Touch, D; pain, P | Lost | Absent | Spastic | +++ | ++++ | 75 | Improved |
| 37 | M | 3 yrs. | 2 wks. | Acute retention to paralysis..... | Touch, P; pain and temp., 0 | Lost | Increased | Lost | ++ | +++ | 58 | Improved |
| 27 | M | 2 yrs. | 2 wks. | Numbness; paralysis; incontinence..... | Absent | Lost | Absent | Lost | ++++ | ++++ | 138 | Died |
| 33 | M | 10 yrs. | 3 wks. | Pain in back; numbness; paralysis; incontinence | Absent | Lost | Increased | Lost | ++++ | ++++ | 85 | Improved |
| 32 | M | Denied | 10 days | Numbness; difficult urination; paralysis..... | Absent | Lost | Absent | Lost | +++ | Neg. | 40 | Unimproved |
| 39 | M | 1 yr. | 10 days | Weakness; numbness; retention; paralysis... | Diminished | Lost | Absent | Lost | ++++ | ++++ | 68 | Died |
| 32 | M | 3 yrs. | 1 wk. | Dysentery 1 week; paralysis and retention.... | Right leg, 0; left leg, P | Feeble | Increased | Spastic | +++ | ++++ | ? | Improved |
| 26 | M | Denied | Over night | Paralysis and retention..... | Absent | Lost | Absent | Spastic | ++++ | ++++ | 46 | Died |
| 27 | M | 1 yr. | 7 days | Numbness; weakness; paralysis and retention | Normal | Feeble | Increased | Spastic | ? | ? | ? | Improved |
| 31 | M | 2 yrs. | Over night | Paralysis, retention and constipation..... | Normal | Lost | Increased | Spastic | Neg. | Neg. | 2 | Improved |
| 57 | M | Denied | 3 wks. | Numbness; retention of urine; constipation; paralysis | Normal | Feeble | Increased | Normal | ++++ | ++++ | 17 | Improved |
| 40 | M | 4 yrs. | 2-3 days | Paralysis; incontinence ..... | Normal* | Fair | Increased | Normal | ++++ | ++++ | 14 | Improved |
| 40 | M | 1 yr. | 11 days | Numbness; difficult urination; paralysis..... | Absent | Lost | Absent | Lost | ++++ | ++++ | 147 | Unimproved |
| 37 | M | 1 yr. | 15 days | Numbness; unsteadiness; paralysis..... | Much diminished | Lost | Absent | Lost | +++ | +++ | 247 | Unimproved |
| 32 | M | 1 yr. | 7 days | Numbness; weakness; constipation and retention | Diminished | Feeble | Increased | Spastic | ? | ? | ? | Improved |
| 45 | M | 1 yr. | 10 days | Numbness; difficult walking; incontinence.... | Diminished | Feeble | Increased | Lost | ++++ | ? | ? | Unimproved |
| 32 | M | 2 yrs. | 17 days | Difficulty in walking; paralysis; incontinence | Diminished | Lost | Absent | Lost | ++++ | ++++ | 70 | Improved |
| 40 | M | 16 mos. | 10 days | Difficulty in walking; retention; paralysis... | Normal | Feeble | Increased | Lost | ++++ | ++++ | 13 | Improved |
| 35 | M | 14 mos. | 3 wks. | Pain in back; retention and constipation; weakness | Touch and vib., P; pain and temp., D | Feeble | Increased | Lost | Neg. | Neg. | 11 | Improved |
| 24 | M | Denied | 8 days | Numbness and soreness; weakness; retention; paralysis | Normal | Feeble | Increased | Spastic | ++++ | ? | ? | Improved |
| 31 | M | 2 yrs. | 8 days | Numbness; paralysis; incontinence..... | Much diminished | Lost | Increased | Spastic | ++++ | ++++ | 40 | Improved |
| 39 | M | Denied | 1 wk. | Difficult urination; weakness; numbness; paralysis | Diminished | Weak | Increased | Spastic | ++++ | ++++ | 350 | Unimproved |
| 45 | M | Denied | 17 days | Numbness; weakness; retention; constipation | Diminished | Weak | Increased | Spastic | +++ | ++ | 90 | Improved |

* First seen 80 days after onset; 0, absent; P, present; D, diminished; ?, not recorded.

in cross section supplied by the diseased vessels, the syphilitic virus having, we presume, no particular predilection for any group of vessels.

The motor component was always involved, and the paralysis when seen immediately after the development of the paraplegia, especially in cases in which the signs were those of a transverse lesion, was usually of a flaccid type. In such cases the loss of all deep tendon reflexes and of plantar response, with retention of urine and feces, corresponded to the condition of so-called "spinal shock," the duration of which was rather variable in our few cases. We also observed among our cases that in the acute type in which we felt the lesion was purely thrombotic, the period of flaccidity was considerably shorter (as judged by the return of reflexes and spasticity in recovered cases) than in the subacute or chronic lesions in which it extended over a very much longer period without any sign of supervening spasticity. Furthermore, in cases in which the sensory function was not entirely destroyed and the paralysis was not absolute, we usually found increased deep tendon reflexes, Babinski sign and clonus, and hypertonicity of the muscles. The difference in the severity of the vascular lesions is probably the explanation of these variations in reflex phenomena, as is indicated in the recent experiments on transverse cord lesions by Hunter and Royle,[14] who believe that "vascular disturbance of varying degree was responsible for the variations in the degree and nature of the reflex activity of the isolated spinal cord."

## DIAGNOSIS

Little difficulty will be encountered in recognizing a syphilitic paraplegia in cases in which there is a clear history of primary lesion substantiated by serologic findings, but in a country where syphilis is as prevalent as in China and positive Wassermann tests are accordingly so frequently reported, one must be somewhat guarded not to overlook lesions due to other diseases coincidental with the syphilitic infection. In the apoplectic form, a hemorrhage, either extramedullary or intramedullary, could not easily be distinguished from a thrombosis, but hematomyelia outside of traumatic cases is a rare condition and can be diagnosed only at necropsy, as recorded by Williamson [15] and Fabritus,[16] unless the hemorrhage communicated with the subarachnoid space. A benign tumor of the cord may give rise to rapid symptoms, but again such a phenomenon is rare. Moreover, Spiller [5] calls our attention to metastatic

14. Hunter, J. I., and Royle, N. D.: Symptomatology of Complete Transverse Lesions of the Spinal Cord, Australian J. Exper. Biol. & M. Sc. **1**:57-72, 1924.

15. Williamson, R. T.: Spinal Thrombosis and Hemorrhage Due to Syphilitic Disease of the Vessel, Lancet **2**:14-16 (July 7) 1894.

16. Fabritus, quoted by Cadwalader, W. B., in Onset of Spinal Paralysis, Arch. Neurol. & Psychiat. **6**:541, 1921.

carcinoma (involving the dura in one, and the vertebrae in the other of his cases) which developed symptoms of a sudden paraplegia not by compression but by interference with the spinal circulation. In two cases of acute paraplegia from Pott's disease of the vertebrae reported by Cadwalader,[17] no evidence of compression was found. Spiller here agrees with Cadwalader that the lesion is the result of thrombosis of the vessels due to extension from the diseased bony structure. Fabritus [16] also described a case with pathologic findings of softening of the cervical cord from thrombosis of veins and hemorrhage in the anterior median fissure associated in life with fever and symptoms of an acute infection. Such a case was also recently seen in our clinic in a young nonsyphilitic man who gave a history of a sudden paraplegia, and in whom no cause could be found other than an acute tonsilitis with fever and leukocytosis. The symptoms and manifestations referable to the cord and the throat rapidly subsided, and the patient walked out of the hospital unaided three weeks after entry. On no other basis than that of a thrombosis can we interpret the sudden paralysis and the remarkable improvement, and on the strength of a negative syphilitic history and laboratory findings, together with the evidence of fever and the presence of an acute pyogenic infection, we must regard this case as one of acute pyogenic transverse myelitis. Cases of paraplegia also occur occasionally during pregnancy or parturition, and often no cause is ascertainable. Cerebral paraplegia from hemorrhage about the paracentral [18] lobule of the motor cortex or thrombosis of the superior longitudinal sinus will produce lesions similar to a spinal one, but such cortical or subcortical lesions may be differentiated from the lower type by cerebral symptoms such as the disturbances of consciousness which do not accompany the latter. Finally, embolic lesions can occur from a vegetative endocarditis, empyema, pulmonary abscess, or other conditions, but such paraplegia is rare and can readily be diagnosed with the evidence of a primary focus. At any rate, whatever the underlying cause may be, the mechanism of acute nontraumatic paraplegia is conceded by most investigators to be thrombotic.

### PROGNOSIS

While admitting that the prognosis of acute syphilitic paraplegia is grave, I do not agree with Cole [1] or Lambright [19] that it usually termi-

17. Cadwalader, W. B.: Sudden Onset of Paralysis in Pott's Disease, Am. J. M. Sc. **141**:546, 1911.

18. Wilson, G.: Crural Monoplegia and Paraplegia of Cortical Origin, Arch. Neurol. & Psychiat. **10**:669 (Dec.) 1923.

19. Lambright, G. L.: Report of a Case of Acute Syphilitic Myelitis with Ascending Paralysis, J. A. M. A. **84**:1178 (April 18) 1925.

nates fatally, or with Jauch [20] that "complete or even partial recovery from acute myelitis is rare." Woods,[6] Maxwell [7] and others here in the East have witnessed many a dramatic recovery. In my short experience here, I have seen three such cases of miraculous improvement, and in the outpatient follow-up work. I have been in touch with several cases, especially one which showed no residual evidence of any cord lesion two years after the attack of paraplegia. Besides, two cases of tetraplegia, both syphilitic in origin, may be added to the list of improved or recovered.

Our statistics show death in six cases, in only seven a condition worse at discharge than at entry, and in twenty-one a varying degree of improvement from return of all sensation and reflexes to regaining of considerable motor power and sphincter control. The percentage of our deaths in acute and subacute cases is only 17.7 per cent.

The prognosis, however, especially in the acute cases, depends on the rapidity with which the circulation of the affected area may become reestablished, and the resistance of the individual to secondary infections. Early twitchings or involuntary movements are favorable indications for both life and function; whereas, late return, say after two weeks or more, of sensation, reflexes, movement or automatic bladder leads to a poor outlook, death eventually intervening from intercurrent infections. Many of our improved cases progressed to a chronic stage, a condition showing some return of sensation, frequently complete, slight power with weak or increased reflexes, automatic sphincters and bedsores healing under care. In these cases, the ultimate recovery of motor function is unlikely, and the prolongation of life is largely dependent on the resistance of the patient and good nursing.

## TREATMENT

No attempt will be made to discuss the routine treatment of syphilis and the medical complications from trophic disturbances. Only the apparent value of antisyphilitic treatment needs consideration.

The rapid recovery in some of our cases, I believe cannot be entirely attributed to the administration of arsphenamine or mercury, but largely to the reestablishment of the blood supply of the depleted areas of the cord. A collateral circulation in the cord would best explain the cases of remarkable improvement, oftentimes beginning before arsphenamine was given. Credit is often mistakenly given to the prompt use of arsenicals. For instance, Cole [1] claims the recovery of his patient resulted "through the use of arsphenamine and mercury," and Maxwell [7] states that "these cases (transverse myelitis) lend themselves especially to salvarsan treatment." My opinion is that the recovery, if it occurs

20. Jauch, F. J.: Case of Acute Myelitis with Recovery, Lancet **2**:510, 1923.

at all, will take place in spite of any treatment, but the progress or recurrence of the syphilis can probably be checked by vigorous anti-syphilitic treatment. Further damage to the vessels and meninges is without doubt often prevented by the administration of arsphenamine and mercury.

The relative rarity of this type of syphilitic disease of the spinal cord in America and in Europe today may well be due to early prophylaxis, resulting from finer diagnostic methods and popular education. The high incidence now in China corresponds to that of 1895 in foreign countries when Spiller made his estimation. Whether this type of syphilitic infection will likewise diminish through early treatment of the disease, time alone will determine.

SUMMARY

Rapidly developing paraplegia of syphilitic origin is a common neurologic symptom in China.

A study of thirty-four cases distinguishes two groups: (1) an acute type which develops either over night or within forty-eight hours, accompanied by a flaccid paralysis with total loss of sensory function below the lesion, with sphincter disturbances, and vasomotor changes; (2) a subacute type which develops more insidiously, associated more often with a spastic paralysis with increased reflexes, more or less disturbances in sensation, sphincter troubles and trophic changes.

The pathologic condition underlying these lesions, in the acute cases, is always thrombosis of one or more important spinal vessels with secondary changes in the cord, and in the subacute cases, is also one of thrombosis but with a more widespread meningomyelitis.

Recovery is by no means rare. In general, the disease is not rapidly fatal; but the prognosis as to function in protracted cases is grave.

Reestablishment of the circulation is largely responsible for the cases of recovery.

The use of arsphenamine is necessary to cure the underlying syphilis and to prevent, if possible, further damage to the nervous system.

# THE ROSE BENGAL TEST FOR LIVER FUNCTION

## WITH PARTICULAR REFERENCE TO ITS USE IN THE THERAPY OF SYPHILIS *

N. N. EPSTEIN, M.D.
AND
J. E. RAUSCHKOLB, M.D.
CLEVELAND

Recent advances made in the study of the functional activity of the liver, by means of various tests, have stimulated the interest of the entire medical profession. Of particular note, perhaps, has been the use of dyes which are eliminated solely by the liver through the bile passages. The dyes used for this purpose include phenoltetrachlorphthalein, rose bengal, bromsulphalein, indigo carmine, methylene blue, congo red and others. Of this number, phenoltetrachlorphthalein and rose bengal have been more thoroughly investigated and have lent themselves to clinical use.

It is but natural that the syphilologist should be among the first to determine the efficiency of these tests because of the frequency of hepatic complications seen in the syphilitic clinic. Rosenthal [1] reports that cases of jaundice were eight and eight-tenths more frequent in the syphilitic clinic at Johns Hopkins Hospital than in the medical clinic during the same period. In this work we have applied the rose bengal liver function test to various types of syphilitic patients and to the complications occurring during antisyphilitic therapy.

### HISTORICAL

In 1923, Delprat [3] showed that rose bengal, a fluorescein dye, is eliminated entirely through the bile from the blood stream of dogs. He

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* From the Department of Dermatology and Syphilology of the Western Reserve University Medical School and the Cleveland City Hospital.

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* The rose bengal used in this work was obtained from the National Aniline and Chemical Co., Inc., Pharmaceutical Division, New York.

1. Rosenthal, S. M.: Phenoltetrachlorphthalein Test for Hepatic Function: Recent Studies with the Author's Method, J. A. M. A. **83**:1049-1053 (Oct. 4) 1924.

2. For the sake of convenience, we will use the term liver function to indicate the result of the test.

3. Delprat, G. D.: Studies on Liver Function: Rose Bengal Elimination from the Blood as Influenced by Liver Injury, Arch. Int. Med. **32**:401-410 (Sept.) 1923.

noted the existence of a constant rate of elimination in normal dogs, and that there was a marked delay in the elimination of the dye in dogs with liver injury, the result of chloroform poisoning. Clinical studies on the dye were then carried on at the University of California Hospital during the years 1924 [4] and 1925.[5] The liver function test was studied in patients with no evidence of hepatic disease, in others with cirrhosis of the liver, in obstructive jaundice, in catarrhal jaundice, in metastatic malignancy, in congestive heart failure and in cholecystitis. Through this work a normal curve of elimination of the dye was established. It was shown conclusively that rose bengal is retained in the blood stream of patients with known liver disease for longer periods of time than in normal persons. These findings were checked by clinical, operative and postmortem examinations.

## THE DYE

Rose bengal, tetra-iodotetrabrom fluorescein, is a crystalloid reddish powder which dissolves readily in water or physiologic sodium chloride. It is nontoxic when injected into dogs in a dosage as high as 0.2 Gm. per kilogram and is very well tolerated by human beings. It can be sterilized repeatedly without change, but we have observed that its color fades slowly if exposed to bright sunlight for long periods of time. The dye is inexpensive and readily obtainable. The dye is almost entirely eliminated with the bile although occasionally small traces occur in the urine, especially in cases showing an abnormal retention of the dye in the blood stream. Normally, none of the body fluids or tissues become tinged with the dye when it is injected intravenously, except the blood plasma, the liver and the intestines. The dye normally appears in the duodenal contents of man from fourteen to thirty minutes after its intravenous injection.

We have noted no serious toxic reactions although occasionally slight nausea with sweating has occurred during or shortly after the injection. No rise of temperature has been noted in our cases. In no instance has thrombosis or sclerosis of the vein occurred. In one case, following an extravasation of the dye, the patient complained of slight burning for a few moments, but there was no thrombosis of the vein or injury to the surrounding tissues. There has been no noticeable reaction even in patients with severe liver disease.

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4. Delprat, G. D.; Epstein, N. N., and Kerr, W. J.: A New Liver Function Test: The Elimination of Rose Bengal When Injected Into the Circulation of Human Subjects, Arch. Int. Med. **34**:533-541 (Oct.) 1924.

5. Kerr, W. J.; Delprat, G. D.; Epstein, N. N., and Dunievitz, M.: The Rose Bengal Test for Liver Function: Studies on the Rate of Elimination from the Circulation in Man, J. A. M. A. **85**:942-946 (Sept.) 1925.

### TECHNIC

We have modified the technic of the test slightly from that originally described. A complete discussion concerning the underlying principles of the test may be found in the original reports.[6] It seems advisable to report in detail those changes which we have instituted.

With the usual preparation for intravenous medication, a vein in the cubital fossa is selected and a medium sized needle inserted. Record syringes, 10 cc., and needles were used exclusively in this work. Ten cubic centimeters of blood is withdrawn and transferred to a centrifuge tube, marked no. 1, containing 0.4 cc. of 2 per cent potassium oxalate solution made up in physiologic sodium chloride, which is inverted once gently. Rough handling may cause some hemolysis of the blood. The patient and blood specimens are kept in a subdued light to prevent hemolysis as a result of the photodynamic action of the dye.[7]

The needle is left in situ and 10 cc. of a 1 per cent solution of rose bengal is injected slowly. When 5 cc. has been injected, the time is noted and the injection completed. We have used the dose 10 cc. of a 1 per cent solution, 100 mg., of rose bengal in all the adults and proportionately less for children. The syringe with which the injection is made is discarded and a clean syringe containing from 3 to 4 cc. of sterile physiologic sodium chloride is attached to the needle in the vein. The needle is kept free from blood clot by frequent injections of small amounts of the sodium chloride solution. At the end of one and one-half minutes, blood is withdrawn slowly, so that when two minutes have passed the syringe contains 5 cc. of blood. The blood is then transferred to centrifuge tube no. 2, containing 0.2 cc. of the potassium oxalate solution, and the tube is inverted once gently. The syringe is washed with physiologic sodium chloride, refilled with the saline solution and again attached to the needle in the vein. In a similar manner, an eight minute specimen is obtained and transferred to centrifuge tube no. 3, containing 0.2 cc. of the potassium oxalate solution.

This procedure differs from the original technic in that a four minute specimen is not taken, and that 0.2 cc. of potassium oxalate solution, 2 per cent, made up in physiologic sodium chloride instead of 2 cc. of 2 per cent potassium oxalate solution is used. This has the obvious advantage of requiring less manipulation of the vein, of necessitating less laboratory work and of giving as much information.

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6. Footnotes 4 and 5.

7. Schmidt, C. L. A., and Norman, C. F.: Protection Afforded to Red Cells Against Hemolysis by Eosin, J. Infect. Dis. **27**:40 (July) 1920; J. Gen. Physiol. **6**:681 (July) 1922.

The blood specimens nos. 1, 2 and 3, control, two minute and eight minute, respectively, are centrifuged until the supernatant plasma is clear. The color in tubes 2 and 3 is then compared with a standard solution of the dye made up as follows:

Five cc. of the plasma in tube no. 1 (control specimen) is added to 5 cc. of a 0.0075 per cent solution of rose bengal, made up by adding 0.75 cc. of a 1 per cent solution of rose bengal to 100 cc. of water. This is thoroughly mixed, and 5 cc. of the resultant solution is added to 15 cc. of water. The original 5 cc. of the 0.0075 per cent solution of rose bengal is thus diluted three times.

The plasma in tubes no. 2 and 3 is diluted twice by pipetting 1 cc. of plasma and adding it to 3 cc. of water. These dilutions are used for convenience in colorimetric determinations. The diluted plasmas are then compared with the diluted standard solution in a Hellige colorimeter. Since the plasma of tubes 2 and 3 are diluted in the same manner, the relationship between the color of each specimen will be constant.

*Calculation of Results.*—The method of calculation, as originally described, required that the blood volume of each patient be calculated so that the colorimetric readings of the various patients might be compared with a standard. The arbitrary standard selected was an individual with a blood volume of 7000 cc. who had received 100 mg. of the dye, giving a resultant solution of 19.1 per cent of the standard prepared as above. The colorimetric reading of the plasma of the two minute specimen, after being corrected for dilution by the oxalate solution and for the solid elements of the blood which contained no dye, was reduced to 19.1 per cent at the expense of the blood volume. In other words, the colorimetric reading of specimen no. 2 was reduced to 19.1 per cent. This was done in every instance so that, since the blood volume does not concern us here, we have reduced the 2 minute colorimetric reading directly without calculating the blood volume. Thus we have kept the same arbitrary standard but eliminated most of the calculation. The eight minute colorimetric reading is then compared with the standard (19.1 per cent) by the following fraction.

$$\frac{\text{8 minute reading}}{\text{2 minute reading}} \times 191\% = 19.1\%$$

For example:

We find the 2 minute colorimetric reading is 70 and the 8 minute colorimetric reading 35; then to reduce this to standard conditions we simply calculate as follows.

$$\frac{35}{70} \text{ or } \frac{1}{2} \times 19.1\% = 9.5\%$$

since 19.1 per cent is the highest concentration of the dye possible under standard conditions, we will refer to this figure as 100 per cent

retention of the dye in the blood stream. Since we are interested only in how much dye the liver can excrete in 8 minutes, the 8 minute reading, reduced to the standard conditions will determine whether a patient has a normal or abnormal liver function.

The upper limit of normal as previously established is 11.5 per cent for the 8 minute colorimetric reading. Regarding 19.1 per cent as 100 per cent retention of the dye, the upper limit of normal will be 60 per cent retention, and we will consider an 8 minute reading of more than 60 per cent as abnormal and denoting impaired liver function.

This report is based on a total of 252 tests applied to various types of syphilitic patients classified in table 1.

*Early Syphilis—Primary Stage.*—Twenty-seven cases of proved primary syphilis were studied, the average 8 minute reading, that is, the liver function, being 49 per cent—well within the upper limit of

TABLE 1.—*Classification of the Tests Performed*

| | Stage of Disease | | | | | Syphilis and Pregnancy | Complications of Arsphenamine | |
|---|---|---|---|---|---|---|---|---|
| | Early Primary | Early Secondary | Late | Hereditary | Latent | | Dermatitis | Jaundice |
| No. of tests | 27 | 112 | 45 | 4 | 8 | 8 | 8 | 40 |

normal 60 per cent retention of the dye. A slightly abnormal retention was noted in three instances with readings of 65 per cent, 63.5 per cent and 61 per cent, respectively. The latter cases were late primary cases with 4 plus blood Wassermann reactions. There is apparently no alteration of the normal liver function in early primary syphilis.

*Early Syphilis—Secondary Stage.*—One hundred and twelve tests were performed in ninety-seven cases of active secondary syphilis, the average 8 minute reading being 52.5 per cent with a range of from 78 per cent to 36.5 per cent. Four cases showed from 2 to 6 per cent impairment of liver function, and five, an impaired function varying from 8 to 18 per cent. In general, 5 per cent of this group showed a marked impairment of liver function, while 4 per cent had a moderate delay in the excretion of the dye.

A classification of these patients as to the presenting cutaneous eruption (table 2) was made in an attempt to determine whether the type or the severity of the eruption was related to any impairment of liver function. While patients with extensive small papular eruptions had the greatest impairment of liver function, moderate and severe degrees of impairment were noted in patients with other types of eruption. Rosenthal [1] found a slight degree of abnormal liver function in

90 per cent of syphilitic patients with a generalized eruption, but his series of cases was rather small. In general, it may be said that the patients with secondary syphilis who have a marked constitutional reaction to their disease are most likely to have some disturbance of liver function.

*Late Syphilis.*—Forty-five tests were completed on forty-two patients with various lesions, classified in table 3. In two patients with gummatous processes, impaired liver function, 13 per cent in one and 9 per

TABLE 2.—*Classification of Secondary Syphilis as to Eruption*

| Eruption | No. of Cases | Average 8 Minute Reading, Percentage | Range of Readings, Percentage | Percentage Abnormal | Percentage Impairment |
|---|---|---|---|---|---|
| Papular | 40 | 53 | 38 to 78 | 5 marked<br>10 slightly | 18 to 8<br>7.5 to 1.2 |
| Roseola | 18 | 51 | 46 to 62 | Very slight variation | Not over 2 |
| Recurrent papular | 6 | 58 | 54 to 69 | 16 | 9 |
| Follicular (lichen syphiliticus) | 5 | 55 | 43 to 68.5 | 20 moderate | 9 |
| Condyloma lata or mucous patch | 8 | 51 | 37.5 to 60 | 0 | 0 |
| Leukoderma | 2 | 63 | 61 to 66 | 100 moderate | 1 to 6 |

TABLE 3.—*Late Syphilis*

| Lesion | No. of Cases | Average 8 Minute Reading, Percentage | Range of Readings, Percentage | Percentage Abnormal | Percentage of Impairment of Liver Function |
|---|---|---|---|---|---|
| Gumma in various locations | 17 | 52 | 42 to 73 | 27.7 | 5 to 13 |
| Central nervous system syphilis and tabes dorsalis | 16 | 50 | 37 to 62.5 | 6 | 2.8 |
| Vascular syphilis | 4 | 51 | 40.5 to 63 | 25 | 3 |
| Ulcerocrustaceous | 2 | 78 | 58 | 0 | 0 |
| Miscellaneous | 3 | 58 | 52 to 62 | 66 | 1 to 2 |

cent in the other, was noted. On physical examination no evidence of hepatic disease was found in either of these cases. The others in this group were normal or slightly abnormal.

*Latent Syphilis—No Clinical Signs.*—There were eight cases in this group, the average 8 minute reading being 50 per cent, with a slight impairment of 2.2 per cent in one case.

*Syphilis Associated with Pregnancy.*—Eight patients in the secondary stage of syphilis associated with pregnancy varying from six months antepartum to two months postpartum, showed an average retention of 52.5 per cent of the dye at 8 minutes. Three patients had a slight degree of impairment.

*Congenital Syphilis.*—Four patients with hereditary syphilis, all of whom had had considerable antisyphilitic therapy and varying in age from 6 to 16 years, had an average liver function of 51 per cent. None showed impairment.

Our findings in the average run of patients who had been under antisyphilitic therapy for several years showed no alteration from the normal liver function. One patient with an extensive psoriasis who had developed arsenical keratoses as a result of taking solution of potassium arsenite (Fowler's solution) over a period of forty years, had a normal liver function.

TABLE 4.—*Dermatitis Developng During Antisyphilitic Therapy*

| Case | Preparation Used | Stage of Disease | 8 Minute Reading, Percentage | Percentage of Impairment | Clinical Notes |
|---|---|---|---|---|---|
| 1 | 18 weekly injections of bismuth oleate | Primary | 57 | 0 | A severe exfoliative dermatitis which persisted for 4½ months; his course was marked by several severe exacerbations of his dermatitis; bismuth deposits were present in the gluteal and lumbar regions; patient recovered |
| 2 | Arsphenamine, total 2.4 Gm. | Late | 50 | 0 | A severe vesicular exfoliative dermatitis; patient recovered after a stormy course |
| 3 | Arsphenamine, total 0.8 Gm. | Secondary | 50 | 0 | A severe dermatitis exfoliativa with high fever and stupor; patient recovered after a stormy course |
| 4 | Neo-arsphenamine, 6 injections | Late | 67.5 | 7.5 | Patient entered hospital with an extensive papulopustular exfoliative dermatitis; she developed a bronchopneumonia, with exitus; necropsy showed bilateral bronchopneumonia, syphilitic aortitis, miliary tuberculosis and marked cloudy swelling of the viscera |
| 5 | Arsphenamine, total 2.8 Gm. | Secondary | 67.5 | 7.5 | Moderate generalized dermatitis which cleared completely within 7 days; patient has been an alcoholic for many years |
| 6 | Arsphenamine, total 1.9 Gm. | Late | 50 | 0 | A mild dermatitis on the extremities which cleared rapidly after cessation of the arsphenamine medication |
| 7 | Arsphenamine, total 0.8 Gm. | Secondary | 52.5 | 0 | A very mild dermatitis which cleared up rapidly |
| 8 | Arsphenamine, total 1.2 Gm. | Secondary | 47 | 0 | A moderate generalized dermatitis which cleared up rapidly after cessation of the arsphenamine medication |
| 9 | Arsphenamine, total 0.8 Gm. | Secondary | 55 | 0 | A very mild dermatitis which cleared up rapidly |
| 10 | Neo-arsphenamine, 1 injection | Primary | 50 | 0 | Patient developed a purpuric eruption on both lower extremities which cleared up gradually within 18 days |

## COMPLICATIONS ARISING DURING THE COURSE OF ANTISYPHILITIC THERAPY

*Dermatitis.*—One of the most serious accidents which may occur during the course of antisyphilitic therapy is the development of an extensive generalized exfoliative dermatitis. Any degree of dermatitis occurring during arsphenamine therapy should be regarded as a danger

signal. We have studied the liver function in this type of case in the hope of finding some relationship between the dermatitis and liver dysfunction. The group included ten instances of this complication, four of which were very severe dermatitis exfoliativa cases, while six had a mild or moderate dermatitis. Table 4 shows the findings.

No close relationship was found in our cases between arsphenamine or bismuth dermatitis and liver dysfunction. Both the very severe and the milder cases showed an elimination of the dye within the normal limits—though possibly the upper limits. In two patients with moderate impairment of liver function, other factors, namely, cloudy swelling of the liver in one instance, probably secondary to tuberculosis, and alcoholism in the other, may have somewhat affected the results.

*Jaundice.*—Probably one of the most common complications arising during the course of antisyphilitic therapy is the development of icterus. This may be preceded by general pruritus, vague abdominal complaints such as distention, belching, nausea and loss of appetite, weakness and occasionally enlargement and tenderness of the liver. It may be very mild in character or very severe, terminating, in exceptional instances, fatally.

Scott and Pearson [8] divide the cases of arsphenamine jaundice into two groups; those who develop jaundice from one to seven days after the last injection of arsphenamine, and those who develop jaundice from twenty-two to one hundred and thirty-two days after the last injection. The dosage of arsphenamine seemed to play little part in the production of the icterus. In our series of cases, the icterus followed the last injection of arsphenamine in from four to seven days in four instances, and from six weeks to three months in three. None of the patients received more than 2.5 Gm. of the arsphenamine.

Piersol and Bockus [9] and S. M. Rosenthal,[1] using phenoltetrachlorphthalein, carefully studied liver function in cases of arsphenamine jaundice. O'Leary [10] and Broun [11] applied this test to several patients whom they observed for several months. In general, our findings agree with these observers' except in a few instances.

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8. Scott, G. O., and Pearson, C. H.: Syphilitic and Arsenical Jaundice, Am. J. Syphilis **3**:628 (Oct.) 1919.

9. Piersol, G. M., and Bockus, H. L.: Comparative Studies in Liver Function by Some of the Later Methods, J. A. M. A. **83**:1043-1049 (Oct.) 1924.

10. O'Leary, P. A.: Postarsphenamine Jaundice, M. Clin. N. Amer. **8**:1203-1213 (Jan.) 1925.

11. Broun, C. O.: Toxic Hepatitis Following Salvarsan Administration, M. Clin. N. Amer. **7**:989-997 (Nov.) 1923.

TABLE 5.—*Liver Function in Cases of Jaundice Developing During Arsphenamine Therapy*

| Case | Date | 8 Minute Reading, Percentage | Percentage Abnormal | Clinical Notes |
|---|---|---|---|---|
| 1 | 9/22/25 | 65.5 | 5.5 | The patient, a white man, aged 54, with vascular syphilis had had 2.7 Gm. of arsphenamine between 4/4/25 and 6/20/25. He received no more arsphenamine until 9/12/25 (0.3 Gm.). One week later the patient became icteric. He complained of slight nausea, belching, loss of appetite and tenderness in right upper quadrant of abdomen. The liver was slightly enlarged |
| | 9/27/25 | 73 | 13 | Jaundice deeper; subjectively the same |
| | 10/ 2/25 | 73 | 13 | Condition the same |
| | 10/ 8/25 | 73 | 13 | Liver more tender; patient rather weak; intensely jaundiced |
| | 10/13/25 | 78 | 18 | Jaundice intense; subjectively the same |
| | 10/18/25 | 73.5 | 13.5 | Condition the same; test probably an indication of improving liver function |
| | 10/28/25 | 47 | 0 | Jaundice clearing; patient greatly improved |
| | 11/ 3/25 | 42 | 0 | Jaundice about gone; patient feels fine |
| | 11/15/25 | 46.5 | 0 | No evidence of liver disease |
| | 11/29/25 | 43 | 0 | No evidence of liver disease |
| | 12/13/25 | 47.5 | 0 | No evidence of liver disease |
| | 1/ 3/26 | 36 | 0 | No evidence of liver disease |
| | 2/28/26 | 45 | 0 | No evidence of liver disease |
| 2 | 11/22/25 | 67 | 7 | A white woman, aged 27, developed a moderate icterus 6 weeks after the last injection of arsphenamine; except for slight loss of appetite patient felt fairly well; liver not enlarged |
| | 12/ 6/25 | 46 | 0 | No jaundice; feels fine |
| | 1/24/26 | 50.5 | 0 | No evidence of liver disease |
| 3 | 10/14/25 | 52 | 0 | A white man with secondary syphilis had received 0.3 arsphenamine |
| | 10/30/25 | 50 | 0 | Patient had developed a papular erythematous eruption after 3 injections of arsphenamine, total 1 Gm.; eruption cleared in 3 days; patient is slightly icteric; complains of nausea, loss of appetite and weakness |
| | 11/ 1/25 | 63.5 | 3.5 | Jaundice moderate |
| | 11/ 8/25 | 61 | 1 | Patient feels better; icterus clearing |
| | 11/15/25 | 44 | 0 | Patient well |
| 4 | 12/30/25 | 62.5 | 2.5 | Six weeks following 6 injections of neo-arsphenamine (? dose and intervals), a white woman, aged 36, developed a moderate icterus; liver palpated 2 finger lengths below costal border is slightly tender; complains of loss of appetite and slight nausea |
| | 1/ 3/26 | 71.2 | 11.2 | Jaundice deeper; patient subjectively the same |
| | 1/10/26 | 44 | 0 | Jaundice about gone; feels well |
| | 1/17/26 | 52 | 0 | No evidence of liver disease |
| 5 | 2/15/26 | 73 | 13 | A white woman, 2 months postum developed a very extensive dermatitis exfoliativa and a moderate icterus after 1.4 Gm. arsphenamine; onset began 5 days after the last injection of arsphenamine; liver slightly enlarged and tender; temperature normal; complains of loss of appetite |
| | 2/20/26 | 74.5 | 14.5 | Patient worse; temperature of 40 C. (104 F.); dermatitis much more extensive; face and eyelids swollen and general edema of the entire body; urine normal; lumbar puncture normal |
| | 2/27/26 | 66.5 | 6.5 | The dermatitis has subsided somewhat; temperature lower; jaundice about the same |
| | 3/ 3/26 | 66 | 6 | Patient about the same; she seems out of danger |
| | 3/ 7/26 | 55 | 0 | Patient feels greatly improved; temperature normal; jaundice slight |
| | 3/13/26 | 45 | 0 | Dermatitis about well; slight icterus persists |
| | 3/26/26 | 52 | 0 | No evidence of liver disease |
| 6 | 3/ 3/26 | 72 | 12 | A colored man, aged 54, developed a mild icterus 3 months after a series of 6 injections of arsphenamine; complains of loss of appetite and weakness |
| | 3/ 7/26 | 42 | 0 | Jaundice has about disappeared; patient feels very well |
| 7 | 8/27/25 | 83 | 23 | Patient seen only once during the course of an intense icterus which followed the third of a series of 3 arsphenamine injections; complained very little; the liver was not enlarged; patient made an uneventful recovery |
| 8 | 8/30/25 | 57 | 0 | The patient was first seen 3 months after an icterus which persisted for 3 weeks and followed shortly after the last of a series of 8 injections of arsphenamine; no evidence of liver disease, and the patient felt very well |
| 9 | 9/27/25 | 46 | 0 | Three months ago, the patient became jaundiced while under therapy for primary syphilis; icterus cleared rapidly within 3 weeks; he has had no trouble since and has felt very well |
| 10 | 12/14/25 | 84 | 24 | Patient developed a moderate jaundice while under malaria therapy for taboparesis; he had had cyclic chills every other day from 11/28/25 to 12/12/25; quinine medication was started because of icterus; patient had a severe toxic delirium throughout course of therapy; liver slightly enlarged |
| | 12/20/26 | 76 | 16 | Delirium marked; jaundice clearing slightly |
| | 12/31/26 | 63 | 3 | Jaundice clearing rapidly; delirium unchanged |
| | 3/ 1/26 | 47 | 0 | Patient very much improved as to his psychosis; jaundice gone |

COMMENT

Study of this group of cases revealed interesting findings. The rate of elimination of the dye ran parallel to the clinical condition. In case 1, the patient was observed over a period of five months with frequent tests of his liver function, which corresponded closely to his clinical condition. During the period of liver disease, the elimination of the dye was definitely delayed, but several days before the icterus had faded perceptibly a normal liver function was obtained; with complete recovery the test was repeatedly within normal limits.

In case 5, the patient had a severe dermatitis exfoliativa combined with hepatitis. The test yielded valuable information in following the course of her clinical condition. It was noted that the liver dysfunction did not increase when the dermatitis became more severe.

The other cases of jaundice, mild in character and transient in duration, exhibited hepatic dysfunction, the test approaching normal as they improved.

TABLE 6.—*Cases of Acute Syphilis with Impaired Liver Function*

| Case | Stage of Disease | Date | Therapy | 8 Minute Reading, Percentage | Percentage of Impairment | Clinical Notes |
|---|---|---|---|---|---|---|
| 1 | Active secondary | 8/16/25 | None | 61 | 1 | Patient had a marked small papular eruption; moderate malaise; severe laryngitis; no fever |
| | | 8/22/25 | 1 arsph. | 62.5 | 2.5 | Marked Herxheimer reaction |
| | | 10/10/25 | 8 arsph. | 45 | 0 | Feels well |
| 2 | Active secondary | 3/ 2/26 | None | 67 | 7 | Sparse maculopapular eruption; slight malaise; no fever |
| | | 3/ 3/26 | 2 arsph. | 43.5 | 0 | Feels very well |
| 3 | Active secondary | 3/ 2/26 | None | 68.5 | 8.5 | Sparse roseola; moderate malaise; no fever |
| | | 3/ 5/26 | 1 arsph. | 39 | 0 | Greatly improved |
| 4 | Active secondary | 2/28/26 | None | 62 | 2 | Large roseola eruption; no fever |
| | | 3/ 7/26 | 3 arsph. | 42 | 0 | Eruption had disappeared; patient feels fine |

Two cases were studied three months after recovery from an attack of icterus, both patients showing normal findings.

It is of interest to mention an instance of jaundice developing in a patient under malaria therapy for taboparesis, in which there was a marked delay in the excretion of the dye and a gradual return to normal with improvement of the clinical condition. This apparently indicates that hemolysis is not always entirely responsible for jaundice occurring during the course of malaria, and that liver disease possibly plays an important rôle in its production.

CASES OF ACUTE SYPHILIS WITH IMPAIRED LIVER FUNCTION

During the past year, we have encountered seven acute cases of syphilis manifesting peculiar symptoms as far as liver dysfunction was concerned and yet showing no clinical manifestation of the disease on

physical examination. We consider them important enough to mention them in particular. As shown in table 6, the first four patients were not especially ill from the syphilis, yet their liver function was impaired from 8.5 per cent down to a point just above normal limits. On administration of arsphenamine, this dysfunction responded at once.

The three other cases which we would place in this same group showed a more unusual clinical picture. There was a more marked constitutional reaction to their disease, as evidenced by severe malaise, weakness, headache, general aching pains and in two of them temperatures around 39 and 40 degrees.

TABLE 7.—*Cases of Secondary Syphilis with Marked Constitutional Reaction*

| Case | Date | 8 Minute Reading, Percentage | Percentage Abnormal | Clinical Notes |
|---|---|---|---|---|
| 1 | 9/25/25 | 78 | 18 | A white man, aged 45, presented an extensive small papular eruption of secondary syphilis; he complained of marked malaise, headache and generalized aching pains; he was weak and listless; temperature normal; no jaundice or evidence of hepatic disease |
| | 10/ 2/25 | 62.5 | 2.5 | Patient had received 2 injections of arsphenamine, 0.3 and 0.4 Gm., respectively; much improved |
| | 10/14/25 | 46 | 0 | Patient feels perfectly well |
| 2 | 1/22/26 | 68.5 | 8.5 | A colored man, aged 21, presented a florid syphilis, secondary stage; he had an extensive follicular eruption, an iritis and was very toxic; he had a temperature of 39 C. (102.2 F.); complained of marked malaise and weakness; no jaundice or other evidences of liver disease |
| | 1/28/26 | 54.5 | 0 | Patient had received 2 injections of arsphenamine with great improvement; no fever |
| | 2/ 3/26 | 45.5 | 0 | Continued improvement; iritis much better; had received 3 injections of arsphenamine |
| | 2/14/26 | 45.5 | 0 | Has had 5 injections of arsphenamine; feels entirely well; discharged from the hospital |
| 3 | 1/28/26 | 73 | 13 | A colored man, aged 25, had suffered with a continued fever for 4 months; he was very weak, but not emaciated; physical examination was entirely negative except for a generalized papulopustular eruption; the blood Wassermann test was 4 plus; no jaundice or other evidence of hepatic disease; diagnosis, syphilitic fever |
| | 2/ 3/26 | 60.5 | 0.5 | Has received 5 injections of arsphenamine, 0.2 each; feels much better; temperature normal; eruption clearing |
| | 2/ 7/26 | 49.5 | 0 | Much stronger; patient left the hospital 3 days later |

Each patient presented a different type of eruption. There were no symptoms or physical signs indicating hepatic disease, and yet, as we see from table 7, one of them had an 18 per cent impairment, another 8.5 per cent and the third 13 per cent. It is evident that the capacity of their livers to eliminate rose bengal from the blood stream was much impaired. The pathologic condition responded at once to arsphenamine therapy.

In our experience with the rose bengal test, such marked changes in liver function have been encountered only in the presence of definite liver disease. Moreover, of the seven patients, three at least exhibited such marked constitutional reaction to their syphilis that in spite of the absence of jaundice or of other physical signs of liver disease, we are inclined to regard these patients as having definite syphilitic liver changes—possibly an acute syphilitic hepatitis. We would urge clinicians to watch more carefully for this manifestation.

SUMMARY

No definite change from the normal liver function was found in patients with early primary syphilis. Of the group with secondary syphilis, the highest degree of impaired liver function was noted in those with an extensive small papular eruption, but this seemed dependent more on the extent of the eruption and the severity of the constitutional reaction of the patient than on the type of cutaneous manifestation present. The liver function was not impaired in one case of acute syphilitic nephritis.

Of the patients with late syphilis, one with a gumma of the pharynx and one with a gumma of the rectum showed the greatest retention of the dye found in this group. We had opportunity only to examine one case of gumma of the liver, and this was after the patient had received some arsphenamine therapy. The test was normal at that time. The cases of latent and congenital syphilis showed little change from the normal. Of the instances of secondary syphilis associated with pregnancy, three patients had a slight impairment of liver function.

No constant relationship was noted between arsphenamine or bismuth dermatitis and liver dysfunction, although the retention of dye in these cases was usually in the upper limits of normal—approaching abnormal. Arsphenamine jaundice was constantly associated with a definite delay in the elimination of rose bengal from the blood stream. With clinical recovery the liver function became normal. No permanent impairment of liver function was noted in patients who were studied several months after recovery from arsphenamine icterus.

One patient who had developed jaundice while under malaria therapy for taboparesis showed marked retention of the dye, but elimination returned to normal as the icterus disappeared.

Seven patients with active secondary syphilis, and three of them in particular having a marked constitutional reaction to their disease, showed definite impairment of liver function although accompanied by no icterus or other physical signs of liver disease. The dysfunction gradually returned to normal as the clinical condition improved under arsphenamine therapy, and we are inclined to classify the process as an acute syphilitic hepatitis.

CONCLUSIONS

Latent hepatic disease occurring in patients in the various stages of syphilis can be detected by means of the rose bengal liver function test.

We were unable from our study to show that arsphenamine dermatitis is an absolute indication of liver insufficiency.

Arsphenamine jaundice is constantly associated with definite retention of rose bengal in the blood stream. With clinical recovery, the

liver function returns to normal. There is no permanent change in liver function following clinical recovery from an arsphenamine hepatitis.

Acute syphilitic hepatitis probably sometimes occurs during the secondary stage without physical signs pointing to liver disease.

We frequently found the rose bengal liver function test a valuable indicator as to the prognosis in cases of arsphenamine icterus. Moreover, we believe it reveals to us cases of acute syphilitic hepatitis which cannot be diagnosed in any other manner. The test is an adjunct in the treatment of syphilitic patients.

## DISCUSSION

Dr. William J. Kerr, San Francisco: It seems to me that this is a very important contribution. For some time we have been interested in the liver function tests, particularly in the one which was used in this study. The dye is one which is eliminated practically entirely by way of the liver. That which is not eliminated by the liver is apparently destroyed somehow in the blood stream. It is interesting that Dr. Carl Schmidt of the department of chemistry has discovered that it is the size of the molecule which determines its route of elimination from the body. The dye contains six halogens, and tests have shown that dyes of this content are eliminated through the liver, so we feel that in the rose bengal test we have a dye that is better for this purpose than any other.

The work of the essayist is of great interest, because we have wanted to know for a long time whether exfoliative dermatitis was associated with any derangement of the liver. It has been noted that in some instances dermatitis occurred in association with jaundice, and in others where there was no jaundice. We find that the liver may be damaged, the kidney may be damaged, the skin may be involved, or the central nervous system, so it might be expected that this would be the case here. We would not expect to find impairment of the liver function, necessarily, when the skin was involved. I felt, and I think Dr. Cole agreed, that we would find involvement of the liver function with exfoliative dermatitis, but this has been proved not to be the case. It has been proved that the jaundice appearing in the syphilitic patient after arsenical treatment is due to damage of the liver. In the same way the jaundice may be a catarrhal jaundice or there may be destruction of the cells which causes the jaundice. It is of interest that with impaired function treatment may be carried on, and the permeability of the liver for the dye may be restored. This is interesting, because it is similar to what we find in the kidney where we have a syphilitic process, giving large amounts of albumin, and very little else, and large doses of arsphenamine or other treatment will rapidly clear up the condition in the kidney.

I consider these studies of great value because they will help us to understand the jaundice in hepatitis and other cases, and I believe will put us on a firm basis for therapeusis.

Dr. W. H. D. Goeckerman, Rochester, Minn.: I would like to know whether Dr. Epstein in his work with this drug has seen any evidence that the drug might photosensitize the patient, or that there may be any other untoward effects. The literature indicates that it is next to hematoporphyrin as a photodynamic agent. I have been tempted to use the drug in the treatment of certain dermatoses, but have refrained from its internal use because of my impression that it is not without its dangers.

DR. J. E. RAUSCHKOLB, Cleveland: I believe that the rose bengal test indicates before the clinical symptoms whether the patient will get better or worse. We found repeatedly in jaundice cases that before the jaundice or the toxicity increased or decreased in intensity the test revealed this prior to the clinical findings.

DR. E. A. PURDUM, Hot Springs, Ark: I should like to have the essayist tell us something about the continuation of treatment after the development of an arsphenamine jaundice; whether in the cases in which he found the liver function to be very good, according to the test, he continued the treatment without any very untoward results.

DR. N. N. EPSTEIN, Cleveland: Dr. Schmidt and Dr. Norman of the University of California have studied the photosensitivity of these dyes and their action on the red blood cells of the known organism. We have taken all the precautions we could to protect the patients from bright sunlight after the use of these dyes, because of these researches, but in some instances in which there was a slip-up of the plan or in the technic, and the patient was exposed to bright sunlight, we have had no reaction; so we no longer keep the patients in subdued light. In the first case we did we found considerable hemolysis in the red blood cells which prevented reading of the colorimetric index; so we have kept the blood in reduced light while carrying out the test. The patients have had no untoward effects. There has been some vomiting occasionally, but no serious toxic effects have been noted. In one case in which I accidentally infiltrated around the vein, there was slight burning, but no thrombosis or sclerosis of the tissues occurred.

As to Dr. Purdum's remarks, the treatment of the arsphenamine icterus, of course, demands careful administration of the arsphenamine, but after considerable rest Dr. Cole believes that it is permissible to give a small injection. We have never seen a recurrence of the icterus, but extreme care is taken, with every precaution. The technic is not difficult. It is simply the intravenous procedure, and the colorimetric readings after some experience are very easy.

# HAIR DYES AND THEIR TOXIC EFFECTS

## CLASSIFICATION AND DESCRIPTION

LAWRENCE K. McCAFFERTY, M.D.
NEW YORK

### CLASSIFICATION AND APPLICATION OF DYES

Vegetable dyes were the first hair dyes, then metals, and finally the synthetic organic dyes. First, we have the organic vegetable colorings which are best represented by henna, indigo, wood extracts (logwood, redwood, pyrogallol and tannin) and herbs such as sage and camomile. Second, metallic preparations, such as silver, lead, copper, cobalt, tin, bismuth, cadmium, nickel and iron. Third, compound dyestuffs utilizing mordants, which are a mixture of a vegetable dye such as henna with a metallic preparation such as copper or iron. Fourth, aniline derivatives and other synthetic organic compounds.

1. *Vegetable Compounds.*—Henna, the best known example of this group, is a small plant which grows chiefly in Morocco, Algiers, Tunis, Egypt, Arabia and India. The method of using henna dye has always been the same. The dried leaves and stems are ground to a powder and made into a thick paste with water. The hair is thoroughly washed and dried and the paste is applied directly to the hair. The resulting color of the hair depends on the time of contact with the paste. Henna has but one color, and this is red. Hair which is slightly dyed with henna has only a light red reflection. Ten minutes imparts a reddish tinge to brown hair; one hour produces a bright red. White and blonde hair acquire peculiar orange tones which are artificial in appearance and unattractive. Henna dye does not penetrate the hair shaft; it merely coats it, but the color which is produced is reasonably permanent. Of all dyes, it is perhaps one of the least harmful to the system. However, when it is used repeatedly over long periods of time, it has a tendency to make the hair brittle.

Indigo, a plant similar to henna, is rarely, if ever, used alone as a hair dye. The ancient Persians combined henna and indigo for dyeing their hair, and by varying the proportions they managed to produce a whole series of browns and blacks. The active principle of the indigo plant is indigotin. Indigotin is a dark blue substance which is insoluble in water, ether, alcohol and most organic solvents. The best natural indigo has always been obtained from India, although most of the material used today is made synthetically. The henna-indigo combination is now rarely used as a hair dye, because of the length of time required, and because it is rather difficult to determine the exact propor-

tions of each that will produce the desired colors. (Colman [1] gives a method of procedure which will not be outlined here.) Combinations of henna and indigo are harmless, but since they coat the hair, it becomes brittle after the long continued use of these dyes.

Wood Extracts: Decoctions made from the bark, roots, stems, leaves and nuts of various trees have been used as dyes. Logwood and redwood extracts were formerly used extensively, but more recently they have been abandoned because of the limitations of the shades obtained. The liquid obtained by boiling the green leaves and both the ripe and unripe shells of walnuts, has commonly been used as a dye. It is called a progressive dye because a number of applications is necessary to obtain any noticeable effect. The most important active principle of the nut extracts is pyrogallol, commonly called pyrogallic acid. When pyrogallol absorbs oxygen it is converted into a brown dyestuff of uncertain composition. If pyrogallol and tannin are used for a certain period of time, they may become poisonous, and symptoms of intoxication by absorption may develop.

An infusion made from the flowers and leaves of camomile is supposed to preserve the color of light hair, but its efficacy is doubtful. The infusion of sage, another herb, is supposed to darken light hair, but the action is slow and the color uncertain; therefore, it is no longer considered of much value. Rhubarb, in the alkaline extraction of its roots, was formerly used to produce a golden color and to brighten the shades of blond hair, but its use was always limited, and has now ceased. Practically all the wood and herb extracts, especially nut galls, sage and camomile, have been used successfully in certain localities because they are easy to obtain, and as home preparations are perfectly safe. The disadvantages from their use are the length of time involved in making so many applications and the difficulty of producing the proper shade.

2. *Metallic Preparations.*—The first metals mentioned in history for the purpose of dyeing hair were silver, copper, mercury, tin and lead. For dyeing hair these metals must be in the form of a dilute solution of one of their salts. The dyeing action is supposed to depend on the combination of the metal with the sulphur in the hair, producing a metallic sulphide. The hair may be said to act as a reducing agent, liberating the metal which combines with the sulphur to form a sulphide which is deposited on the shaft of the hair. Almost all the metallic preparations are progressive dyes, because their application must be repeated several times before the deposit on the hair is sufficient to darken it. The variety of shades from metallic preparations is limited.

(*a*). Lead Dyes: Lead, in the form of lead acetate (sugar of lead),

1. Colman, J.: Haarfärbemittel, in Joseph, Max: Handbuch der Kosmetik, Leipzig, Veit & Co., 1912, pp. 441-459.

has been for years the chief ingredient of many commercial hair dyes. When this solution is applied to the hair it combines chemically with the sulphur in the hair and produces lead sulphide, which is deposited on the hair shaft as a black film. Many commercial hair dyes on the market today consist of a solution of lead acetate containing free sulphur. When these two ingredients come in contact with each other on the hair, lead sulphide is produced. Several years ago special lead combs were commonly used for dyeing the hair. By continually combing the hair with such a comb it became dark because of the formation of the lead sulphide. The final color obtained from the use of lead preparations is always a dull, lifeless black which often wears off to purple. The chief disadvantage of lead dyes is their tendency to produce lead poisoning; for this reason it should be prohibited.

(*b*). Silver Dyes: Silver, in the form of silver nitrate, is the basis of several other widely known hair dyes. When silver nitrate alone is applied to the hair, it will dye it gradually; but since its action is very slow, it is usually combined with a developer. Both pyrogallol and sodium thiosulphate have been used as developers for the silver solutions.

In making the application of a silver dye, the hair is thoroughly washed. If the hair is saturated first with a solution of silver nitrate and then with pyrogallol, the silver solution is reduced; the silver then combines with the sulphur in the hair and forms a film of silver sulphide on the hair. If sodium thiosulphate or sodium sulphide is applied to hair which is saturated with silver nitrate, the silver sulphide forms at once on the hair. The color produced by the developers varies from a light brown to black, depending on the concentration of the silver solution. If the silver nitrate is dissolved in ammonium hydroxide instead of water, blond and brown colors may be produced; in general, the more ammonia used, the lighter the shade. Silver preparations, with or without ammonia, are sold as progressive dyes principally for home use. They may appear either as a single solution with a small package of the powdered developer, or as two solutions. Silver preparations are less harmful than those of lead, but serious cases of argyria may develop. Furthermore, the colors are unnatural, and in time the hair takes on a greenish tinge or an unpleasant metallic luster.

(*c*). Copper: The principle here is the same as with silver. Copper sulphate (blue vitriol) or copper chloride, with or without ammonia, is the basic substance; pyrogallol is the developer. The end result is the formation of copper sulphide which coats the hair with a dark brown or black deposit. Because of recognized poisonous properties, copper-pyrogallol preparations for the hair have long been prohibited legally in certain European countries.

(*d*) Tin and cadmium were formerly used in preparations for blonde hair. The soluble salts of both metals are poisonous; they are seldom, if ever, used today. Bismuth preparations produce colors varying from blonde to brown shades in proper solutions. Cobalt compounds in dilute solution are sometimes used to produce light shades. As with silver, the color depends on the concentration of the solution; however, the final color is black. Both cobalt and bismuth salts are poisonous. Nickel, which is similar to cobalt, is used for the dark shades; its soluble salts are also poisonous. Iron salts were formerly used, but they have been almost completely discarded because their color is not permanent and wears off rapidly to a dull gray.

(*e*) In this same group we may mention potassium permanganate. It is very soluble in water, and when the bright purple solution comes in contact with organic matter it is reduced, changing in color from purple to brown. It was originally used, as a progressive dye, but its action is so slow that it is found only in the most antiquated formulas.

In brief, one may say that all metallic hair dyes must be considered potentially dangerous. When used for certain periods of time, absorption is bound to take place. Usually before any untoward symptoms are noticed, the patient is so saturated with the metallic poison that the case may be serious. This chapter in medicine is too well known to be further emphasized here. All metallic hair dyes should be prohibited.

3. *Compound Dyestuffs with Mordants.*—These preparations correspond to what were known in the Orient hundreds of years ago as Rastiks. They are dyes composed of two distinct substances, namely, a vegetable product and a metallic salt. One of the earliest of these preparations for the hair was made as follows: powdered nut galls were roasted with an oil; the oily paste was mixed with water, and a certain amount of iron and copper oxide was added; the whole mixture was kept in a closed vessel for some time, and during this period, the metallic oxides acted on the pyrogallol in the nut galls; a poultice was made from this mixture and was left on the head for several hours.

The principal use today of this class of dyestuffs is in the textile industry. The natural dyeing power of the vegetable product (logwood, redwood, etc.) is developed by the addition of various metallic mordants.

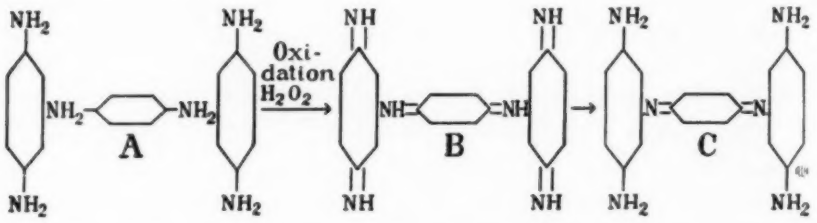
The compound hennas which are so commonly used as hair dyes belong to this class. The various shades of henna, "brown henna" and "black henna," are produced in this way, since the dyeing action depends principally on the pyrogallol and the metal; the henna may be said to act only as a carrier. Frequently there is only sufficient henna to allow the manufacturer to use the name "henna dye."

4. *Synthetic Organic Dyes.*—This group perhaps represents the most widely used dye preparations today. Many modern organic dyes are

derived from aniline. Its importance as a dye was recognized shortly after its discovery, but the difficulty of obtaining it from natural sources prevented its rapid development.

In 1854, a compound called para-phenylene-diamine was prepared from para-nitro-aniline. Its discoverer, Hoffman,[2] in collaboration with Muspratt, did further work on isolating and purifying it in 1863, but it was not practically used at that time.

Para-phenylene-diamine is a white, crystalline substance which is soluble in water and most organic solvents. It was first used as a dye for furs; it was shown to act on an entirely new principle as it penetrated the hair shaft instead of coating the outside. Because the shades produced were excellent fast colors, it was soon used as a dye for human hair. From Germany and France its use spread rapidly to all the countries of Europe, and its popularity increased tremendously as time went on because of its ease of application, its beautiful varied shades and the permanence of its colors. Unfortunately, however, it was not long before its poisonous effects were noticed among the workers in the fur dye industry.




Transformation of para-phenylene-diamine into Bandrowski's base. *A* represents three molecules of para-phenylene-diamine; *B*, three molecules of di-imine; *C*, one molecule of Bandrowski's base.

The dyeing action of para-phenylene-diamine depends on its oxidation. It readily absorbs oxygen from the air, but the oxidation is usually hastened by the addition of hydrogen peroxide, which quickly transforms it into a dark compound called Bandrowski's base. The intermediate product formed in transforming para-phenylene-diamine into Bandrowski's base is a substance called quinone-di-imine. According to Erdman,[3] the poisonous action attributed to para-phenylene-diamine is really due to this intermediate product, quinone-di-imine.

Bandrowski's base, which is the end-product of the oxidation of para-phenylene-diamine, is probably a tetra-amido-diphenyl-para-azo-phenylene.

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2. Hoffman, A. W., and Muspratt: Recherches sur les diamines isomerès. Compt. rend. **56**:992, 1863.

3. Erdman, E.: Ber. d. deutschen chem. Gesellsch. **37**:2906-2910, 1904.

On Feb. 1, 1906, the German Federal Council passed a resolution withdrawing para-phenylene-diamine from unrestricted sale, and placed it with the list of poisons. All receptacles containing para-phenylene-diamine and destined for German retail trade must now be marked with the label "poison" in red letters on a white background, and give a statement of the contents. Austria soon passed a similar resolution, and before long, many of the other European countries had followed the example. Manufacturers have resorted to many subterfuges to evade the declaration of para-phenylene-diamine in various hair dyes; one instance is that of placing inside the package a label which reads, "cannot be responsible for any inconvenience resulting from the use of this coloring," etc.

Much research has been done on nonpoisonous hair dyes. Joseph [4] lays great stress on a dye called "Primal," which he considers the best dye in this group of synthetic organic compounds. Its base is para-toluylene-diamine, which is said to be detoxified by the addition of sodium sulphite. It has been described as apparently harmless; nevertheless, certain cases of dermatitis have resulted from its use. Up to the present time we have no synthetic organic coloring for the hair which is entirely nontoxic.

*Other Preparations for the Hair.*—(*a*) Bleaching Agents: In 1818, Thenard discovered hydrogen peroxide. Thiellay was the first to use hydrogen peroxide for bleaching hair; its use has been continued and is now well known. Hydrogen peroxide is principally used in a 3 per cent (ten volume) solution. Because it loses oxygen, the bleaching power decreases on standing, and a fresh preparation should be used each time.

The method of procedure is very simple, and for this reason it is probably used more frequently than any other preparation. The hair is first washed and dried and then saturated with hydrogen peroxide; the liquid remains on the hair until the desired shade is obtained. Its action may be quickened by the addition of a little ammonia, but this brings out a disagreeable reddish tone. When hydrogen peroxide is used in excess, it has the disadvantage of making the hair extremely dry and brittle, causing it to break off very readily on continued application. Sabouraud [5] mentions a woman whose hair broke off as short as a man's after using hydrogen peroxide. Many preparations sold as "washes," "rinses," etc., for blond hair are largely hydrogen peroxide.

The so-called "white henna" (which contains no henna) is "hydrated white magnesia" (a mixture of the oxide and carbonate of

4. Joseph, Max: The Art of Dyeing Hair, Deutsche med. Wchnschr. **50**: 1370-1380 (Oct.) 1924.

5. Sabouraud, R.: Les teintures de cheveux, Presse méd. **36**:899-905 (May) 1924.

magnesium). In use it is mixed with sufficient hydrogen peroxide or peroxide and ammonia to form a paste, and its action is exactly the same as that of hydrogen peroxide.

(*b*) Dye Removers: Dye removers or decolorizers are various substances, such as hydrochloric acid, potassium cyanide or oxalic acid, which are applied to hair that has been unsatisfactorily dyed for the purpose of removing the dye or of lightening the color of the hair. Potassium cyanide is one of our deadliest poisons and should certainly be prohibited. Hydrochloric and oxalic acid may result in serious injury to the patient. They cause the hair to break easily.

## GENERAL SUMMARY

The vegetable colorings which were first mentioned are perhaps the least harmful of all the dyes. The best known example of this group is henna. As far as I can ascertain, henna has never caused a dermatitis. The vegetable colorings only coat the hair; in time they cause it to become lusterless and brittle. Moreover, the shades fade, and the hair often takes on peculiar colors.

It may be said that all of the metallic salts should be considered potentially dangerous and should not be used. Certain modern hair dyes are advertised as compound hennas for the purpose of misleading the public. They actually consist of metallic salts with a little henna, pyrogallol and other vegetable products. Frequently metallic poisoning results from using these mixtures.

The synthetic organic compounds, of which the best known example is para-phenylene-diamine, are relatively new compared with other hair dyes having been used only since 1883. The toxic effect of para-phenylene-diamine has been known for many years. Not everyone is poisoned by it. It has been estimated that one person in one or two hundred is susceptible.

The clinical results from those susceptible to para-phenylene-diamine may be briefly summarized as follows: Usually a few hours after the application of this dye, the scalp and face begin to tingle and itch; from ten to twelve hours later, there is an edema of the scalp with associated inflammation, vesiculation and crusting in areas the size of a dime. This group of symptoms may and usually does extend just beyond the hair line, over the forehead, temporal regions and behind the ears. The person who is unusually susceptible may develop an edema of the eyelids and the face in general. The eyelids may be so swollen that the patient will be unable to see. Occasionally this dermatitis may spread over the entire body. During the past year, I have seen approximately twenty patients who have been poisoned by para-phenylene-diamine, and in each case the symptoms mentioned above have been most pronounced.

with the exception of a dermatitis extending below the neck. If this condition is not treated immediately, the acute symptoms will subside in a week or so, but the pruritus may continue intermittently over several months, and from the continuous scratching the patient will develop a chronic eczema or dermatitis. The treatment which I have found of the greatest value has been wet dressings of boric acid solution on the affected areas and one-quarter unit doses of the roentgen ray to the scalp and face. Usually one or two roentgen-ray treatments will suffice to eradicate the intense symptoms of the condition, and later, by the application of soothing emollients to the scalp and face, the remaining dermatitis will disappear.

The extreme toxicity of para-phenylene-diamine has been demonstrated in animals. It has been proved that from 0.1 to 0.3 Gm. of para-phenylene-diamine per kilogram of the animal's weight will cause death. Some of the early experimenters on animals (Erdmann,[6] Frankel,[7] Dubois and Vignon,[8] Loewy and Colman,[9] Lewin,[10] Kobert,[11] Erdmann and Vahlen [12]) have reported numerous symptoms which occurred when para-phenylene-diamine was absorbed over long periods of time. In human beings who use para-phenylene-diamine hair dyes, dermatitis is the principal toxic result. In the fur-dyeing industry, in which people are subjected to contact with para-phenylene-diamine over long periods of time, such symptoms as headche, nausea, vomiting, anemia, loss of weight, loss of appetite, temporary loss of vision and "fur-dye asthma" have all been observed.

One may also mention here that many furs, stockings and dress goods are dyed with para-phenylene-diamine. The cheaper furs are more likely to cause a dermatitis, because the less expensive furs are not carefully washed. Occasionally the skin may be chafed by the fur, thus permitting the dye to penetrate more easily through the skin. Patients who once develop a dermatitis from a para-phenylene-diamine hair dye are subsequently more susceptible to a dermatitis from furs that are dyed with para-phenylene-diamine. Many of these patients could per-

6. Erdmann, E.: Ztschr. des allg. Osterreichischen Apotheker Vereins **22**, 1906.

7. Frankel, S.: Die Arzneimittel-Synthese, Berlin, J. Springer, 1921, p. 256.

8. Dubois, R., and Vignon, L.: Sur l'action physiologique de la para et de la métaphénylénediamine, Compt. rend. **107**:533, 1888. Etude preliminaire de l'action physiologique de la para et de la métaphénylénediamine, Arch. de Physiol. **2**:255, 1888.

9. Loewy and Colman: Deutsche med. Wchnschr. **37**:926, 1911.

10. Lewin: Traité de toxicologie, Paris, O. Doin, 1903.

11. Kobert: Lehrbuch der Intoxikationen, ed. 2, Stuttgart, F. Enke, 1906, p. 653.

12. Erdmann, E., and Vahlen, E.: Ueber die Wirkungen des p—Phenylendiamins und Chinondümins, Arch. f. exper. Pathol. u. Pharmakol. **53**:401, 1905.

haps have worn the same furs for years if they had not become sensitized to para-phenylene-diamine.

Why some persons are sensitive to small or large quantities of para-phenylene-diamine cannot as yet be answered. Nor can any definite reason be given why certain persons may wear the same fur for several years or use the same hair dye for a long time and then suddenly become sensitive to it. The amount of dye remains the same, but perhaps the resisting power of the skin is decreased. On the other hand, the skin may reach its limit of absorption and the subsequent dermatitis may develop.

## CONCLUSIONS

Vegetable hair dyes, such as henna, are harmless.

All metallic dyes are dangerous.

Compound hennas are dangerous because of the metallic substances which they contain; the amount of henna is slight and acts only as a carrier for the metal.

All synthetic organic dyes, of which the most important member is para-phenylene-diamine, are dangerous.

Bleaches, such as hydrogen peroxide, when freely used may cause the hair to break off.

Dye removers are dangerous and should be prohibited from use in beauty shops.

# CUTANEOUS MANIFESTATIONS OF PROTEIN ALLERGY

GEORGE PINESS, M.D.
AND
HYMAN MILLER, M.D.
LOS ANGELES

Included as a phase of immunity is a contrary state, namely, anaphylaxis, in which the defense mechanism of the body assumes a destructive character. Immune reactions of the body are commonly brought about by the action of and find expression in the elaboration of substances of a protein nature, antigen and antibody. The same holds true in certain self-destructive reactions of the body, such as anaphylaxis. On this common basis of protein reaction the concept of anaphylaxis has come to be regarded as a phase of immunity.

However, both clinically and experimentally many reactions have been observed of a nature similar to anaphylaxis in which proteins apparently take no part. To include these nonprotein reactions and at the same time to emphasize their essential similarity to protein reactions, von Pirquet [1] in 1905 coined a new word, "allergy," which he defined as "an altered reactivity." As is evident, this definition does not limit the use of the word allergy to an altered reactivity to proteins alone. If we wish to so limit its use, we must modify the term to "protein allergy." In the following study we are interested only in those cutaneous lesions which may be considered as due to the latter.

Before attempting to trace the reasons for considering particular skin lesions to be of allergic origin, two striking facts present themselves for consideration.

## ALLERGIC PERSONS AND ALLERGIC MANIFESTATIONS

Tilbury Fox [2] in 1873 said: "Take a given number of persons and apply to their skins the same local irritant and you will have eczema in some and not in others." In other words, Fox recognized that there exists a group of persons with an altered reactivity to substances which are innocuous to the average person. Present knowledge has created the presumption that the members of this group are of an allergic constitution, and that this constitution is in many cases inherited.

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1. Von Pirquet, C.: Allergy, Arch. Int. Med. **7**:259 (Feb.) 1911; **7**:383 (March) 1911.

2. Fox, Tilbury: Skin Diseases 1873, quoted by Highman, W. J.: A Critical Review of Eczema and Dermatitis, J. Cutan. Dis. **34**:259 (April) 1916.

To paraphrase Tilbury Fox: Take a given number of allergic persons and apply to their skins a protein to which all are sensitive, and you will have eczema in some and urticaria in others. This speaks for an underlying similarity between the two manifestations. As will be seen later, it is a demonstration of the common allergic constitution of the persons tested rather than evidence for the diagnosis of two distinct diseases of the skin.

### SKIN MANIFESTATIONS OF PROTEIN ALLERGY

In 1907, Wolff-Eisner [3] expressed the belief that urticaria belongs to the group of manifestations resulting from protein allergy. This belief was in accord with von Pirquet and Schick's [4] findings that serum disease in which urticaria is a prominent symptom is due to an altered reactivity to foreign serum protein. That proteins from food sources might produce urticaria was demonstrated by Smith,[5] who described violent gastro-intestinal symptoms associated with urticaria following the ingestion of buckwheat, and Scofield [6] who noted the same train of symptoms following the ingestion of egg.

It remained for Schloss [7] to apply in a practical manner the findings of the authors mentioned above. Smith had demonstrated a localized skin reaction from the application of buckwheat to the arm of the patient who reacted so violently from its ingestion. Blakely [8] had long before shown that it was possible to identify offending pollens in hay-fever in the same manner. Schloss,[9] following these leads, applied various food proteins to the skin of a patient suffering from giant urticaria, eczema, gastro-intestinal disturbances and asthma. Some of these proteins produced an urticarial wheal at the site of their application. On removing these proteins from the diet, he found that the symptoms disappeared.

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3. Wolff-Eisner: Ueber die Urticaria von Standpunkte der neuren Erfahrungen, Dermat. Ztschr. **14**:164 and 312, 1907.

4. Von Pirquet, C., and Schick, B.: Die Serum Krankheiten, Deuticke, Vienna, 1905.

5. Smith, H. L.: Buckwheat Poisoning, Arch. Int. Med. **3**:350 (May) 1909.

6. Scofield, A. T.: A Case of Egg Poisoning, Lancet **1**:716 (March) 1908, quoted by Schloss: Am. J. Dis. Child. **3**:341 (June) 1912.

7. Schloss, O. M.: A Case of Food Allergy; Idiosyncrasy to Eggs, Almonds and Oats, Due to Anaphylaxis, Arch. Pediat. **29**:219 (March) 1912; A Case of Allergy to Common Foods, Am. J. Dis. Child. **3**:341 (June) 1912.

8. Blakely, C. H.: Experimental Researches on the Causes and Nature of Catarrhus Aestivus, London, Bailliere, Tindall & Cox, 1873; Am. J. M. Sc. **47**: 181, 1874.

9. Schloss, O. M.: Allergy in Infants and Children, Am. J. Dis. Child. **19**: 433 (June) 1920.

Further work was done by Schloss, Blackfan,[10] Talbot,[11] Walker [12] and many others along similar lines. This resulted in the establishment of protein allergy as the etiologic factor in a number of diseases which had long been grouped under the general term of "exudative diathesis." The work of these investigators also led to the development of the use of systematic protein skin testing in diagnosis and rational treatment.

With the establishment of the reliability of this means of diagnosis it was not long before attempts were made to define more clearly those diseases of the skin which properly might be considered due to protein allergy. Thus Turnbull [13] classified as of this etiology eczema, urticaria, prurigo, erythema multiforme, angioneurotic edema and erythema. That this list is too comprehensive, our own observations and those of others indicate. A search of the literature shows that protein skin tests have been made in acne, dermatitis herpetiformes, erythema multiforme, lichen urticatis, pompholyx, pemphigus, purpura hemorrhagica, dermatitis vegetans, prurigo, pruritus ani, psoriasis, eczema, urticaria and angioneurotic edema.

Reference to table 1, which includes all the conditions mentioned except urticaria and eczema, shows that comparatively few positive reactions have been obtained. With the exception of erythema, probably none of the conditions listed are protein allergic in origin. In those instances, for example, acne and psoriasis, in which sensitization to proteins was demonstrated, we feel that the conditions were coincidental with allergy. In our own cases some other allergic condition, usually asthma or hayfever, frequently existed whenever positive skin reactions were obtained (69 per cent of 214 cases which gave positive reactions).

*Angioneurotic Edema.*—As described by Quincke, this condition should not be included with the allergic skin diseases. We agree with Crowder [14] that "typical Quincke's disease with its large, pale, cool, non-itchy swellings is in marked contrast to the usual forms of urticaria and unlike urticaria the question of food seems unimportant as an

10. Blackfan, K. D.: Cutaneous Reactions from Proteins in Eczema, Am. J. Dis. Child. **11**:441 (June) 1916.

11. Talbot, F. B.: Rôle of Food Idiosyncrasies in Practice, New York State J. Med. **17**:419 (Sept.) 1917.

12. Walker, I. C.: Studies on the Sensitization of Patients with Bronchial Asthma. Studies III, IV & V, X to XVII, J. M. Res. **35, 36** and **37,** 1917. Studies VI, VII, VIII, J. Immunol. **2**:227 (April) 1917. Study IX, Am. J. Bot. **4,** July, 1917. Causation of Eczema, Urticaria and Angioneurotic Edema by Proteins Other Than Those Derived from Food. Study XVIII, J. A. M. A. **70**:897 (March 30) 1918.

13. Turnbull, J. A.: Disturbances Caused by Proteins, Boston M. & S. J. **182**: 493 (May) 1920.

14. Crowder, J. R., and Crowder, T. R.: Five Generations of Angioneurotic Edema, Arch. Int. Med. **20**:840 (Dec.) 1917.

TABLE 1.—*Skin Diseases in Which Protein Skin Tests Have Been Made*

| | Acne | | Dermatitis Herpetiformes, | Erythema Multiforme | | Lichen Urticaris, | Pompholyx, | Pemphigus, | Purpura Hemorrhagica, | Dermatitis, | Prurigo | | Pruritus Ani, | Psoriasis | | Dermatitis Vegetans, | Angioneurotic Edema | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Positive | Negative | Negative | Positive | Negative | Negative | Negative | Negative | Negative | Negative | Positive | Negative | Negative | Positive | Negative | Negative | Positive | Negative |
| Authors | 5 | 2 | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | 1 | 3 | .. | .. | 13 |
| Engman, M., Jr., and Wander, W. G.: Arch. Dermat. & Syph. **3**: 223 (March) 1921 | .. | 18 | 11 | .. | 6 | 4 | 4 | 2 | 3 | 9 | .. | .. | .. | .. | .. | 1 | .. | .. |
| Cranston-Low, R.: Anaphylaxis and Sensitization, New York, William Wood & Company, 1925 | .. | .. | 1 | .. | .. | .. | .. | .. | .. | .. | 1 | 3 | .. | .. | .. | .. | .. | .. |
| Schloss, O. M.: Am. J. Dis. Child. **19**: 433 (June) 1920 | .. | .. | .. | 1 | 6 | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | 2 | 12 |
| Coke, F.: Asthma, New York, William Wood & Company, 1923, p. 142 | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | 2 | .. | .. | .. | .. | .. |
| Rackemann, F. M.: Am. J. M. Sc. **163**: 87 (Jan.) 1922 | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | 8 | 7 |
| Highman, W. J., and Michael, J. C.: Arch. Dermat. & Syph. **2**: 544 (Nov.) 1920 | .. | .. | .. | .. | .. | .. | .. | . | .. | .. | .. | .. | .. | .. | .. | .. | 8 | 5 |
| Strickler, Albert: J. Immunol. **1**: 475, (Aug.) 1916 | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | 11 | .. | .. | .. |

etiologic factor." This statement is supported by the results of our protein skin tests. In twelve cases of typical angioneurotic edema which were tested, no positive reactions were obtained. That other authors, as table 1 shows, have reported positive skin reaction in angioneurotic edema, Schloss,[9] Highman,[15] Rackemann,[16] and others, is true. We feel, however, that they have erred in terming as angioneurotic edema what should in reality be termed allergic giant urticaria. Examination of their cases often shows a coincident asthma or hay-fever to confirm this.

*Erythema.*—This condition as the result of protein allergy is best exemplified in serum disease. Its occurrence as a solitary manifestation of a food protein allergy has been rare in our experience. Engman [17] tested six such cases to food proteins and found them all negative. Schloss tested seven and found six negative. We have had only ten cases of simple erythema, and all of these may properly be classified as pollen erythemas comparable to those described by Sutton,[18] Walker,[19] Schloss [9] and Hannah.[20] All were associated with seasonal hay-fever or asthma.

*Urticaria.*—This eruption is commonly if not always of allergic origin. Yet no classification of urticaria has been put forth which takes cognizance of this fact. Sutton's [21] classification, which is typical of many, makes use of such terms as "urticaria acuta," "urticaria factitia" and "urticaria papulosa." The first of these is descriptive of the clinical course, the second is descriptive of the etiology, and the third is descriptive of the anatomic appearance, a sufficient commentary on the fact lost sight of in this classification that urticaria is not a disease but merely the symptom of one, the disease being the allergic constitution.

*Eczema.*—Like urticaria, eczema has usually been classified with regard to the clinical appearance of the various lesions, as Stelwagon [22] has done. This has resulted in such difficulty that eczema has been

15. Highman, W. J., and Michael, J. C.: Protein Sensitization in Skin Diseases; Urticaria and Its Allies, Arch. Dermat. & Syph. **2**:544 (Nov.) 1920.

16. Rackemann, F. M.: Skin Tests with Foreign Proteins in Various Conditions, Am. J. M. Sc. **163**:87 (Jan.) 1922.

17. Engman, M., Jr., and Wander, W. G.: The Application of Cutaneous Sensitization to Diseases of the Skin, Arch. Dermat. & Syph. **3**:223 (March) 1921.

18. Sutton, R. L.: Ragweed Dermatitis, J. A. M. A. **73**:1433 (Nov. 8) 1919.

19. Walker, I. C.: Causation of Eczema, Urticaria and Angioneurotic Edema by Proteins Other Than Those Derived from Food. Study XVIII, J. A. M. A. **70**:897 (March) 1918.

20. Hannah, L.: Ragweed Dermatitis, J. A. M. A. **72**:853 (March 22) 1919.

21. Sutton, R. L.: The Classification of the Urticarias, J. Cutan. Dis. **35**:749 (Nov.) 1917.

22. Stelwagon, Henry W.: Diseases of the Skin, ed. 9, Philadelphia, W. B. Saunders Company, 1905, 259.

described as "the term commonly applied to any wet or scaly inflammation of the skin of the cause or nature of which the observer is ignorant." Eczema, as many writers in the past have realized, is but the external manifestation of some internal disorder. The modern concept of this internal disorder is the allergic constitution.

Erythema, urticaria, and eczema are skin lesions of the same underlying pathology. The frequent observation of their sequence in the order given or of their simultaneous presence in the same person speaks for a difference only of degree, the type of lesion depending on the state of sensitivity of the patient, the character of the skin or the dose of the offending substance.

In view of these facts we feel it to be proper to include erythema, urticaria and eczema under the generic term "allergic dermatitis." This would dispose of the objection made by Highman [23] who in his delightful essays objects to the use of the term eczema in view of its pathologic identity with dermatitis.

*Allergic Dermatitis.*—This condition may be divided into a nonprotein and a protein type. The former is well exemplified in the skin lesions following the administration of such substances as acetyl salicylic acid or arsphenamine or of the application of materials used in the trades as summarized by Knowles [24] and Cranston-Low.[25] The protein type of allergic dermatitis must further be divided into two groups: one in which preliminary sensitization can be proved, as in experimental anaphylaxis, and the other in which no history of such previous exposure to the offending protein seems to be necessary. In the latter group fall the numerous cases of protein allergy demonstrably or presumably sensitive to food or environmental proteins.

Allergy
- Allergic Dermatitis
  - Nonprotein
  - Protein
    - Previous Sensitization
    - No Previous Sensitization

## STATISTICAL STUDY

*Age Incidence.*—In all, 345 persons exhibiting erythema, urticaria or eczema came under our observation. Table 2 shows the distribution of these cases both as to age of onset and age at the time of observation.

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23. Highman, Walter J.: A Critical Review of Eczema and Dermatitis, J. Cutan. Dis. **34**:259 (April) 1916. Eczema and Dermatitis, Arch. Dermat. & Syph. **11**:303 (March) 1925.

24. Knowles, F. C.: Eczema of External Origin and Its Relationship to Dermatitis, J. A. M. A. **68**:79 (Jan. 13) 1917.

25. Cranston-Low, R.: Anaphylaxis and Sensitization, New York, William Wood & Company, 1925.

Of significance in table 2 is the evident preponderance of the disease in the first decade of life. Of the 345 cases, 190 or 55 per cent, date onset before the age of 10 years.

*Heredity.*—A history of allergic disturbance in forbears and siblings was obtained in 41 per cent of the cases studied. This coincides closely with the figures of Adkinson,[26] Cooke and Vander Veer [27] and Spain and Cooke [28] obtained in a study of all types of allergic manifestations. It must be emphasized that heredity transmits the allergic constitution and not the particular clinical type of the disease, nor a sensitization to a particular protein.

*Clinical Types of Allergic Dermatitis.*—Many authors have discussed urticaria and eczema separately. Although it is possible in our series of cases to classify ninety-two cases as eczema only, that is, no other allergic manifestation present, and forty-one cases as urticaria only, this leaves 208 cases which show an association of the two with one

TABLE 2.—*Showing the Age Distribution as to Onset and Time of Observation in 345 Cases of Allergic Dermatitis*

| Age | Onset | Observed |
|---|---|---|
| Under 1 year | 116 | 24 |
| 1 to 10 years | 74 | 113 |
| 11 to 20 years | 44 | 35 |
| 21 to 30 years | 47 | 57 |
| 31 to 40 years | 32 | 54 |
| 41 and over | 29 | 60 |
| Not stated | 3 | 2 |

another or with asthma or hay-fever. In fact, there was an association with asthma or hay-fever in 281 or 81 per cent of our cases, emphasizing that allergic dermatitis is but part of the picture of the allergic constitution.

*Protein Skin Tests.*—These were made on 293 of our 345 cases. Of these, 214 or 73 per cent, gave positive reactions to one or more of the 350 proteins which we used as a routine. This ratio does not differ greatly from that obtained in the two selected groups of eczema or urticaria alone. In the former, of seventy-seven cases tested, forty-eight or 63 per cent gave positive reactions; in the latter, of twenty-four cases tested, fourteen, or 58 per cent, gave positive reactions. These figures are to be compared with those of the authors listed in table 3, from which it may be seen that although positive reactions reach a

26. Adkinson, June: Behavior of Bronchial Asthma as an Inherited Characteristic, Genetics **5**:363 (July) 1920.

27. Cooke, Robert A., and Vander Veer, A., Jr.: Human Sensitization, J. Immunol. **1**:201 (June) 1916.

28. Spain, W. C., and Cooke, R. A.: Studies in Specific Hypersensitiveness XI. The Familial Occurrence of Hay Fever and Bronchial Asthma, J. Immunol. **9**:521 (Nov.) 1924.

high percentage, yet there is considerable divergence in the results by various observers. On the whole, it may be said that positive reactions are obtained in well over 50 per cent of the cases.

TABLE 3.—*Positively Reacting Persons in Groups of Cases of Allergic Dermatitis Collected by Various Authors*

| | Clinical Data | Number of Cases | Percentage Positive |
|---|---|---|---|
| Blackfan (Am. J. Dis. Child **11**: 441 [June] 1916) | Eczema in childhood | 27 | 82 |
| Corper (Am. J. Dis. Child. **29**: 355 [March] 1925) | Eczema under 1 year | 100 | 53 |
| Fox and Fisher (J. A. M. A. **75**: 907 [Oct.] 1920) | Eczema in adults | 60 | 59 |
| Herman (Am. J. Dis. Child. **24**: 221 [Sept.] 1922) | Eczema in infancy and childhood. | 30 | 57 |
| O'Keefe (Boston M. & S. J. **183**: 569 [Nov.] 1920) | Eczema in infancy and childhood. | 70 | 41 |
| Rackemann (Am. J. M. Sc. **163**: 87 [Jan.] 1922) | Eczema in adults | 21 | 19 |
| | Eczema in children | 19 | 42 |
| Ramirez (Arch. Dermat. & Syph. **2**: 365 [Sept.] 1920) | Urticaria in adults | 35 | 17 |
| | Eczema in adults and children | 78 | 38 |
| Schloss (Am. J. Dis. Child. **19**: 433 [June] 1920) | Eczema in infants | 74 | 65 |
| Sidlick and Knowles (Am. J. Dis. Child. **23**: 316 [April] 1922) | Eczema in infancy and childhood. | 23 | 65 |
| Strickler (New York M. J. **109**: 198 [July] 1916) | Eczema in childhood | 46 | 74 |
| White (Boston M. & S. J. **178**: 5 [Jan.] 1918) | Eczema in childhood | 87 | 66 |
| Authors | Allergic dermatitis, under 10 years | 118 | 88 |
| | over 10 years | 175 | 61 |
| | Urticaria only | 24 | 58 |
| | Eczema only | 77 | 63 |

As several of the authors cited have pointed out, positive reactions are most commonly obtained in the younger age groups. This, on the whole, agrees with our findings as summarized in table 4, in which we have arranged the percentage positive reactions obtained in each age group.

TABLE 4.—*Results in Protein Skin Tests in 293 Cases of Allergic Dermatitis*

| Age When Tested | Number of Cases | Positive | Negative | Percentage Positive |
|---|---|---|---|---|
| Under 1 year | 14 | 11 | 3 | 79 |
| 1 to 10 years | 104 | 94 | 10 | 90 |
| 11 to 20 years | 28 | 16 | 12 | 58 |
| 21 to 30 years | 48 | 36 | 12 | 75 |
| 31 to 40 years | 46 | 29 | 17 | 63 |
| 41 and over | 52 | 27 | 25 | 52 |
| Not stated | 1 | .. | .. | .. |
| Total | 293 | 214 | 79 | 73 |

It would be well to point out that several investigators have tested groups of normal children. The positive reactions obtained in these groups were negligible in number. Thus Baker [29] performed 937 tests on normal children and obtained ten positive and eleven doubtful reac-

29. Baker, H. M.: Incidence of Protein Sensitization in the Normal Child, Am. J. Dis. Child. **19**:114 (Feb.) 1920.

tions. On the other hand, 1,322 tests performed on allergic persons showed fifty-five positive and fifty-five doubtful. Blackfan [10] tested forty-three patients without eczema. Only one showed a positive reaction, whereas twenty-seven patients with eczema gave twenty-two positive reactions. Talbot [30] tested 100 normal persons to egg and found only one positive, and here there was some eczema. Peshkin and Rost [31] tested 719 persons without allergic histories, and obtained five positive reactions. They stated that "A normal child exhibiting a positive skin reaction is a potential anaphylactic case and should be regarded as such." With this statement our own experience brings us into entire accord.

*Allergens.*—As a routine, all patients were tested to the 350 proteins derived from foods, pollens, animal emanations, etc. Except for the pollens, these proteins were all prepared as dry powders in our own laboratory and had been proved active by tests on known sensitive patients. The scratch method of testing was used, supplemented by the intracutaneous method when negative reactions were obtained. Retesting was also resorted to in such an event, our findings as a result of such persistent retesting being in accord with those of Schloss,[9] Herman [32] and Low,[33] that is, not uncommonly the patient exhibited an antiallergic state comparable to the anti-anaphylactic state produceable in the experimental animal.

The results of testing, as above outlined, show that positive reactions are most commonly obtained with those proteins which are most commonly met with in the ordinary diet or environment, as Talbot [34] and Walker [35] have pointed out.

*Food Proteins.*—These have been considered, and rightly so, as the most common cause of allergic dermatitis. Of the 214 patients giving positive reactions, 171, or 80 per cent, reacted to food proteins. Only the complete protein molecule can produce sensitization (Wells [36]); that is, allergic dermatitis brought about by the ingestion of food pro-

30. Talbot, F. B.: Eczema in Childhood: Clinical Manifestations—Objective Symptoms, M. Clin. N. Am. **1**:985, 1918.

31. Peshkin, M. M., and Rost, W. L.: The Incidence of Protein Sensitization in the Normal Child, Am. J. Dis. Child. **23**:51 (Jan.) 1922.

32. Herman, H.: A Critical Study of 61 Cases of Asthma and Eczema in Infancy and Childhood Controlled by Cutaneous Protein Sensitization Tests, Am. J. Dis. Child. **24**:221 (Sept.) 1924.

33. Low, R. C.: Cutaneous Sensitization, Brit. M. J. **2**:559 (Oct.) 1921.

34. Talbot, F. B.: The Relation of Food Idiosyncrasies to the Diseases of Childhood, Bost. M. & S. J. **179**:285 (June) 1918.

35. Walker, I. C.: A Clinical Study of 400 Patients with Bronchial Asthma, Boston M. & S. J. **179**:288 (Aug.) 1918.

36. Wells, H. G.: The Chemical Aspects of Immunity, New York, Chemical Catalog Co., 1925, p. 200.

TABLE 5.—*Positive Reactions Obtained in Testing 293 Patients Having Allergic Dermatitis*

| | |
|---|---|
| **Cereals** | |
| Barley | 27 |
| Buckwheat | 21 |
| Corn | 33 |
| Oat | 28 |
| Rice | 25 |
| Rye | 31 |
| Sago | 6 |
| Tapioca | 6 |
| Wheat | 43 |
| **Egg** | |
| Whole | 54 |
| White | 50 |
| Yolk | 24 |
| **Milk** | |
| Whole, cow | 27 |
| Casein, cow | 8 |
| Whey, cow | 16 |
| Whole, goat | 8 |
| Casein, goat | 4 |
| Whey, goat | 6 |
| **Fruits** | |
| Apple | 23 |
| Apricot | 21 |
| Avocado | 8 |
| Banana | 18 |
| Blackberry | 14 |
| Cantaloupe | 26 |
| Casaba | 13 |
| Cherry | 18 |
| Cranberry | 4 |
| Currant | 4 |
| Date | 13 |
| Fig | 11 |
| Grape | 22 |
| Grapefruit | 19 |
| Guava | 4 |
| Lemon | 13 |
| Loganberry | 4 |
| Nectarine | 10 |
| Olive | 5 |
| Orange | 26 |
| Peach | 20 |
| Pear | 15 |
| Persimmon | 11 |
| Pineapple | 21 |
| Plum | 14 |
| Prune | 12 |
| Quince | 2 |
| Raspberry | 18 |
| Strawberry | 7 |
| Tangerine | 4 |
| Watermelon | 10 |
| **Vegetables** | |
| Artichoke | 16 |
| Artichoke, J | 6 |
| Asparagus | 26 |
| Bean, kidney | 22 |
| Bean, lima | 23 |
| Bean, navy | 23 |
| Bean, soy | 5 |
| Bean, string | 20 |
| Beet | 12 |
| Brussels sprouts | 10 |
| Cabbage | 43 |
| Cabbage, red | 12 |
| Carrot | 30 |
| Cauliflower | 26 |
| Celery | 23 |
| Chard, Swiss | 8 |
| Chicory | 2 |
| **Vegetables—Continued** | |
| Cress, water | 7 |
| Cucumber | 16 |
| Egg plant | 12 |
| Endive | 3 |
| Garlic | 7 |
| Kohlrabi | 7 |
| Leeks | 5 |
| Lentil | 20 |
| Lettuce | 21 |
| Lettuce, romaine | 14 |
| Mushroom | 7 |
| Mustard green | 7 |
| Okra | 0 |
| Onion | 22 |
| Parsley | 13 |
| Parsnip | 35 |
| Pea, green | 29 |
| Pea, yellow | 6 |
| Pepper, bell | 5 |
| Pepper, pimienta | 7 |
| Potato, sweet | 16 |
| Potato, white | 33 |
| Pumpkin | 15 |
| Radish, common | 29 |
| Radish, horse | 6 |
| Rhubarb | 17 |
| Rutabaga | 12 |
| Spinach | 25 |
| Squash, banana | 12 |
| Squash, cream | 14 |
| Squash, hubbard | 17 |
| Squash, summer | 12 |
| Squash, zucchini | 5 |
| Tomato | 40 |
| Turnip | 29 |
| Yams | 7 |
| **Nuts** | |
| Almond | 21 |
| Brazilnut | 16 |
| Chestnut | 24 |
| Coconut | 23 |
| Hazelnut | 13 |
| Hickory | 7 |
| Pecan | 21 |
| Peanut | 32 |
| Pinenut | 9 |
| Pistachio | 7 |
| Walnut, black | 26 |
| Walnut, English | 28 |
| **Meats** | |
| Beef | 16 |
| Chicken | 14 |
| Duck | 5 |
| Goose | 11 |
| Lamb | 17 |
| Pork | 14 |
| Rabbit | 7 |
| Squab | 8 |
| Turkey | 8 |
| **Fish** | |
| Anchovy | 8 |
| Barracuda | 12 |
| Bass | 9 |
| Carp | 3 |
| Catfish | 1 |
| Cod, black and white | 5 |
| Codfish | 8 |
| Crab | 21 |
| Flounder | 1 |
| Halibut | 6 |
| **Fish—Continued** | |
| Herring | 4 |
| Lobster | 15 |
| Mackerel | 14 |
| Mussels | 1 |
| Oyster | 7 |
| Perch | 1 |
| Pike | 3 |
| Red snapper | 3 |
| Rock cod | 2 |
| Salmon | 10 |
| Sandab | 1 |
| Sardines | 1 |
| Scallops | 2 |
| Sculpin | 3 |
| Shad | 5 |
| Shrimp | 9 |
| Smelt | 8 |
| Sole | 7 |
| Tuna | 4 |
| Yellowtail | 4 |
| Clam | 7 |
| **Beverages** | |
| Cocoa | 11 |
| Coffee | 4 |
| Tea | 12 |
| **Spices** | |
| Allspice | 0 |
| Bayleaf | 2 |
| Cinnamon | 2 |
| Cloves | 3 |
| Curry | 3 |
| Ginger | 6 |
| Mace | 0 |
| Mustard | 27 |
| Nutmeg | 1 |
| Paprika | 7 |
| Pepper, black | 10 |
| Pepper, cayenne | 11 |
| Pepper, Chile | 2 |
| Sage | 1 |
| **Epidermals** | |
| Chicken feather | 25 |
| Duck feather | 7 |
| Goose feather | 21 |
| Turkey feather | 9 |
| Cat hair | 21 |
| Cattle hair | 10 |
| Dog hair | 7 |
| Horse hair | 15 |
| Rabbit hair | 5 |
| Wool | 12 |
| **Miscellaneous** | |
| Cascara | 6 |
| Cottonseed | 12 |
| Flaxseed | 9 |
| Glue | 33 |
| Henna | 3 |
| Ipecac | 11 |
| Orris | 32 |
| Pyrethrum | 7 |
| Saffron | 1 |
| Beef serum | 1 |
| Horse serum | 6 |
| Silk | 8 |
| Tobacco | 3 |
| Vanilla | 0 |
| Yeast | 7 |
| Pollens (175) | 112 |
| Lycopodium | 8 |

tein predicates the view that unaltered protein must have been absorbed from the gastro-intestinal tract. Schloss and Worthen [37] have reviewed the evidence and have adduced experiments of their own to prove that such is actually the case. Moreover, in the breast-fed infant found sensitive to such foods as eggs, wheat, crab-meat, etc., substances evidently not a part of their diet, Shannon [38] has shown that the mother's milk may contain these substances unaltered. However, the work of Stuart [39] has thrown some doubt on this possibility.

Although it is through ingestion that food proteins most commonly produce symptoms, contact must also be considered. In five cases, we have directly traced a localized dermatitis of the hands to a sensitization to wheat. One of these cases was in a baker and the remainder in housewives.

Only fifty-nine patients, or 23 per cent, of those giving positive reactions reacted to foods alone. The remainder gave reactions to other substances either together with food or without food.

Substances other than food, as Walker [19] has shown, may also be the cause of allergic dermatitis.

*Pollens.*—These gave positive reactions in 112, or 52 per cent, of those reacting. Only twenty-six patients reacted to pollens alone, and of these twenty-two showed symptoms of asthma or hay-fever. Pollen erythema, that is, a seasonal dermatitis due to pollens, was found in ten of the latter. At times we have seen definite aggravation of the lesions of an allergic dermatitis during the course of treatment with pollen antigens. Each such treatment would be followed by an acute, localized exacerbation with a complete subsidence when the course of treatment was ended. Such cases have also been described by Walker.[19]

*Animal Emanations.*—Emanations, such as horse, cat, dog, rabbit, guinea-pig and goat hair and the feathers of chicken, goose and turkey may be the source of protein producing allergic disturbances, as Goodale [40] and Walker [41] have shown. Of the 214 patients giving posi-

37. Schloss, O. M., and Worthen, T. W.: The Permeability of the Gastro-enteric Tract of Infants to Undigested Protein, Am. J. Dis. Child. **11**:342 (May) 1916.

38. Shannon, W. Ray: Demonstration of Food Proteins in Human Breast Milk by Anaphylactic Experiments on Guinea Pigs, Am. J. Dis. Child. **22**:223 (Sept.) 1921. Eczema in Breast Fed Infants as a Result of Sensitization to Foods in Mother's Dietary, ibid. **23**:392 (May) 1922.

39. Stuart, Harold C.: Excretion of Foreign Protein in Human Milk, Am. J. Dis. Child. **25**:135 (Feb.) 1923.

40. Goodale, J. L.: Studies Regarding Anaphylactic Reactions Occurring in Horse-Asthma and Allied Conditions, Ann. Otol. Rhin. & Laryng. **23**:273 (June) 1914.

41. Walker, I. C.: Studies on the Sensitization of Patients with Bronchial Asthma to the Different Proteins Found in the Hair of the Cat and Dog and in the Dandruff of the Horse and to the Sera of These Animals. Study IV, J. M. Res. **35**:497 (Jan.) 1917.

tive reactions, seventy, or 32 per cent, were found sensitive to one or more of the above substances. Inhalation is of course the most common mode of entry of many of these, but contact, such as with wool or mohair (goat hair) may cause a localized or generalized dermatitis. Silk is another substance which may produce an allergic dermatitis through contact. Eight of our cases gave reactions to protein derived from this source.

*Miscellaneous Substances.*—Substances other than those mentioned above have been known to produce allergic dermatitis. One of the most common of these is powered orris root. This substance is part of many face powders, soaps and other scented toilet preparations. Thirty-two patients gave positive reactions to orris root, many of them exhibiting a dermatitis of the face which cleared up on substituting a face powder free from this substance. A severe dermatitis in a beauty parlor worker was definitely traced to orris root used in the administration of dry shampoos.

Orris root is also a constituent of adhesive tape, and we have encountered three patients in whom the application of this tape resulted in a severe localized and at times generalized allergic dermatitis. A similar case was recently reported by Brown,[42] and other cases have been mentioned in the literature without however pointing out that orris root was the offending substance.

Lycopodium gave positive reactions in eight patients. Like orris root, this substance is used in the administration of dry shampoos.

Pyrethrum is a common insecticide. In addition to its use in making up insect powders, it is also often introduced into rugs and hangings before leaving the salesroom. Although no case of dermatitis has been directly traced to this source, its widespread distribution makes it a possible factor. Seven patients with dermatitis gave positive reactions to pyrethrum in addition to other substances.

Flaxseed gave positive reactions in nine patients, but only in one, a druggist, could this substance be said to be more than a possible contributing cause of allergic dermatitis.

This comprehensive summary of the more common substances which may be the source of protein producing allergic dermatitis indicates in some degree the necessity for so painstaking a method of diagnosis as has been outlined. It must be remembered that the allergic constitution can never be cured. Our treatment is palliative in that by determining the cause and removing it from the diet or environment or rendering it innocuous by a process of immunization, we keep the patient more or less permanently symptom-free. Its place in dermatology is therefore not only justified, but necessary.

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42. Brown, W. P.: Sensitization to Adhesive Plaster, Arch. Dermat. & Syph. **12**:69 (July) 1925.

SUMMARY

Protein allergy is a constitutional disturbance characterized by an altered reactivity to foreign proteins.

Allergic dermatitis is one of the manifestations of the allergic constitution.

By means of the protein skin tests it is possible to determine the cause of allergic manifestations.

The information so obtained makes possible the symptomatic cure of the allergic person.

Three hundred and forty-five cases of allergic dermatitis have been studied. The results of this study demonstrate the importance of allergy in dermatology.

1136 West Sixth Street.

# BULLOUS ICHTHYOSIFORM ERYTHRODERMA

## REPORT OF TWO CASES *

WILLIAM H. GOECKERMAN, M.D.
From the Section on Dermatology and Syphilology, Mayo Clinic
ROCHESTER, MINN.

Excluding circumscribed nevi, probably no congenital developmental anomalies of the skin are more common than the multitudinous gradations of ichthyosis, varying from the xerodermatous type of skin, that is merely somewhat dry and scaly, to the keratotic armor of the fetus at birth. Somewhat rare, however, are cases of ichthyosis accompanied by the formation of small and large bullae. Of this type I have observed two unusually interesting cases during the last four years.

### REPORT OF CASES

CASE 1.—A woman, aged 32, had had a cutaneous disease since birth. The skin of the entire body was harsh, dry and thick, and large scales were freely exfoliated. She did not perspire in the ordinary manner when exerting herself, or in rather hot weather without exertion. Bullae varying in size from 1 to 2.5 cm. appeared abundantly on the skin everywhere (fig. 1). When the bullae disappeared, and evidently they did not usually actually rupture, the overlying skin was shed in large flakes (figs. 2 and 3). In certain regions, not necessarily the folds of the body, the skin appeared erythematous, suggesting somewhat that seen in pemphigus foliaceous. The patient had been treated previously by many physicians, without material benefit. Her father was living but not strong. Her mother died at the age of 43 from tuberculosis of the larynx. Two brothers and two sisters were well; a third sister had a disease similar to the patient's. Her parents were first cousins.

After the patient had been examined at the Mayo Clinic, emollient baths, followed by salicylated ointment, were given. This added to her comfort, but of course did not greatly alter the existing state.

A section removed from the left superior iliac region showed no definite pathologic changes in the cutis beyond slight perivascular infiltration and vascular dilatation, and possibly a lack of differentiation in the collagen bundles. There was a low-grade acanthosis of the epidermis, without evidence of edema (fig. 4). In the upper malpighian layers, vesicles appeared in some places with slight accompanying intracellular degeneration and in others as if produced by fluid forced between the layers of the upper rete with compression of the surrounding cells, suggesting a sudaminal origin. There were no signs of true dermatitis (fig. 5).

Neither on potassium hydroxide maceration of some of the scales and vesicular fluid nor after culture were any mycelia found. Staphylococci and streptococci were found as incidental infections. Cultures of the blood for bacteria and

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* Read before the Section on Dermatology and Syphilology at the Seventy-Seventh Annual Session of the American Medical Association, Dallas, Texas, April, 1926.

trichophytons were negative. Neither the blood picture nor studies of the chemistry of the blood revealed any abnormality. The Wassermann test was negative.

CASE 2.—A boy, aged 14, had had a troublesome eruption since the age of 5; his condition prior to that time could not be ascertained. His skin in places was exceedingly thick and hard, some of the scales measuring more than 2.5 cm. in thickness. In other places it was more pliable, and even wrinkled. The folds of

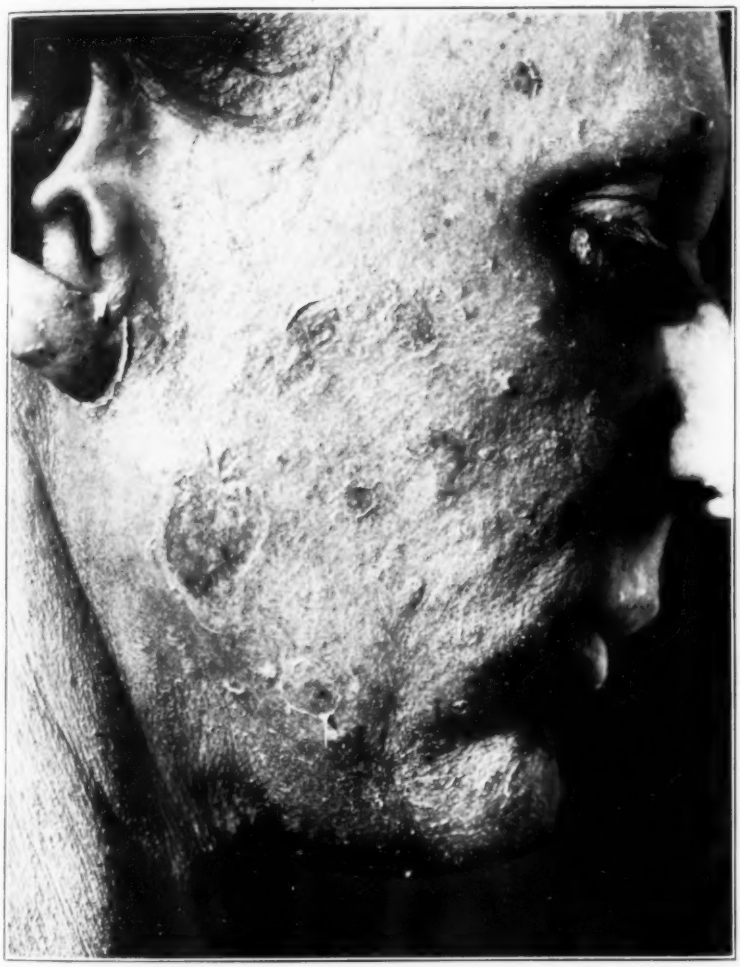

Fig. 1.—The bullous lesions are in the stage of involution.

the elbows and the neck appeared erythematous and definitely ichthyotic, but were reasonably pliable and not affected to the same degree as many other portions (fig. 6). The face was comparatively smooth, but appeared unusually shiny, and somewhat shriveled. There was a moderate degree of ectropion. The palms and soles were markedly hyperkeratotic and appeared verrucous. Bullous lesions with a serous or milky content were everywhere on the body but especially troublesome

on the hands and feet. This patient, as in case 1, did not perspire in the ordinary manner, but the relationship of exertion and heat was not so clear. Moderate pyrexia was noted periodically, which was probably due to lack of proper perspiration and heat radiation. Because of the pyrexia he was carefully examined for

Fig. 2.—Bullous lesions have just subsided and the skin is beginning to exfoliate freely.

tuberculosis, but without the infection being found. The family history was unimportant.

This patient was also given local treatment for symptomatic relief. This contributed to his comfort, but the most benefit was noted from treatment of the feet by the roentgen ray. Almost immediately new bullae ceased to appear in the treated areas. This improvement has lasted for about four years (figs. 7, 8 and 9). He

is fully ambulatory and helps with the farm work, much to the benefit of his general health. Recently the hands and feet were again treated by the roentgen ray with marked benefit. A section for biopsy was not taken in this case. With the exception of the basal metabolic rate, which always hovered about a high normal, routine laboratory findings were negative.

Fig. 3.—Skin exfoliating freely after subsidence of bullae.

## ICHTHYOSIS AND ICHTHYOSIFORM ERYTHRODERMA

It is only necessary to wade through the enormous literature on ichthyosis to become fully aware that the conception of this disease is not clear cut, and yet later articles tend to a broader inclusive view rather than to the subclassification of every cutaneous picture that varies somewhat from that reported by a previous observer. Brocq [1] was confident

1. Brocq, L.: Erythrodermie congenitale ichthyosiforme avec hyperepidermatrophie, Ann. de dermat. et syph. **33**:1-31, 1902.

that he could segregate a group with sufficient characteristics to warrant the term ichthyosiform erythroderma. In this he has had a considerable following. In differentiating this group from ichthyosis vulgaris, Brocq laid most stress on the involvement of the flexures and the rapid growth of hair and nails. Subsequently, in reporting a case with Fernet,[2] he asserted that ichthyosiform erythroderma may be but an attenuated form of ichthyosis congenita and that there may be transitional types. He also no longer regarded the rapid growth of hair and

Fig. 4.—Section from skin; ×30.

nails as a characteristic. Cases otherwise typical of the anomaly may lack this feature.

Riecke[3] subdivides ichthyosis congenita into three groups: (1) ichthyosis congenita gravis, (2) ichthyosis congenita larvata and (3) ichthyosis congenita tarda. He bases this classification on fifty-four cases, two of his own and the remainder from the literature. Group 1 presents the most pronounced epidermal changes in utero, and such a

2. Brocq, L., quoted by MacKee and Rosen, J. Cutan Dis. **35**:347, 1917.

3. Riecke, Erhard: Ueber Ichthyosis congenita, Arch. f. Dermat. u. Syph. **54**:289-340, 1900.

fetus is not viable. In studying groups 2 and 3 it is difficult to see in how the cases essentially differ from those reported as ichthyosiform erythroderma. It is apparent from this author's description that he realizes there is a difference in the degree of the anomaly, but evidently he believes that the fifty-four cases belong in the same group.

Riecke insists that ichthyosis vulgaris is a different type of disease. The differentiating features as seen by him may be given as follows:

| *Ichthyosis Vulgaris* | *Ichthyosis Congenita* |
|---|---|
| Disease inherited | Disease not inherited as a rule |
| Patient develops normally | Patient never thrives |
| General health good, irrespective of degree of cutaneous involvement | General health declines with progress of anomaly |
| Absence of large horny plates | Marked, horny plates |
| Absence of deep fissuring | Fissuring pronounced |
| Face shows little involvement | Face shows prominent involvement |
| Certain sites of predilection | Lesions universal, more or less |
| No involvement of folds | Folds affected |
| Symptoms usually do not show before second year | Symptoms present at birth, or at least during the first few months |

While it is true that ichthyosis congenita, even the milder forms as considered by Riecke, bears but little resemblance to the mildest forms of ichthyosis vulgaris, a pronounced case of the latter cannot be so easily differentiated from a mild type of the former.

Janovski [4] divides ichthyosis vulgaris into three groups: (1) ichthyosis simplex, (2) ichthyosis serpentina, and (3) ichthyosis hystrix. Ichthyosis hystrix is simply the most severe type and does not necessarily denote the linear type as distinguished from the ichthyosis hystrix referred to as such in a number of American textbooks on dermatology. Yet Janovski calls attention to the fact that this type of ichthyosis may assume a linear distribution. Judging from the description he gives, it simply represents a severe type of ichthyosis. It would be difficult to say wherein Janovski's ichthyosis hystrix differs from Riecke's ichthyosis congenita tarda. The classifications employed by these authors may well be cited to illustrate the difficulty of drawing a sharp dividing line.

Jadassohn,[5] in presenting three cases, uses the term ichthyosiform erythroderma. He uses these cases, however, to illustrate how the individual manifestations of the various cutaneous anomalies can combine and how in this manner atypical pictures and seemingly new disease entities arise beside the classical types of this group.

4. Janovski, V., quoted by Bruhns, Arch. f. Dermat. u. Syph. **113**:187-222, 1912.

5. Jadassohn, J.: Familiäre Blasenbildung auf kongenitaler Basis, Verhandl. d. deutsch. dermat. Gesellsch., 1906, pp 381-398.

Lenglet [6] and Jadassohn [7] even go so far as to classify almost all the congenital cutaneous dyskeratoses with ichthyosis. Langlet classifies congenital dyskeratoses under ten headings: (1) agenesis or dysgenesis of hair and nails; (2) functional disturbances of sweat glands and sebaceous glands; (3) keratoderma palmaris and plantaris; (4) ichthyosis foetalis; (5) ichthyosis vulgaris; (6) generalized exfoliation of the new-born; (7) congenital ichthyosiform erythroderma; (8) cutaneous and deep atrophy; (9) congenital bullous affections, and (10) simple epidermolysis bullosa. To these Jadassohn adds three others: (11) pigmentation, (12) anomalies of the teeth and (13) anomalies of the oral mucous membrane.

Fig. 5.—Intracellular and intercellular edema; × 120.

Such observers as Bruhns,[8] Meneau,[9] Jordan [10] and Ingman [11] believe that ichthyosis congenita and ichthyosis vulgaris belong in the same

6. Lenglet, E.: Dyskeratoses congenitales et leurs associations morbides, Ann. d. dermat. et syph. **4**:369-396, 1903.

7. Jadassohn, J., quoted by MacKee and Rosen.

8. Bruhns, C.: Die atypischen Ichthyosisfälle und ihre Stellung zur Ichthyosis congenita und Ichthyosis vulgaris, Arch. f. Dermat. u. Syph. **113**:187-222, 1912.

9. Meneau, J.: De l'ichthyose foetale dans ses rapports avec l'ichthyose vulgaire, Ann. de dermat et syph. **4**:97-114, 1903.

10. Jordan, A.: Ichthyosis congenita s. foetalis, Dermat. Wchnschr. **74**:585-592, 1922.

11. Ingman, A.: Studien über Ichthyosis congenita s. foetalis, Acta derm.-venerol. **5**:125-261, 1924.

group, that they are merely expressions of the same disease in different degrees of severity. Jordan especially brings strong evidence to prove that there is not enough difference to warrant a separate classification and that certain cases closely resemble either of the two forms.

With all the difficulties that are sometimes encountered in classifying an individual case, it would seem that the terms ichthyosis congenita, ichthyosiform erythroderma and ichthyosis vulgaris are of value for

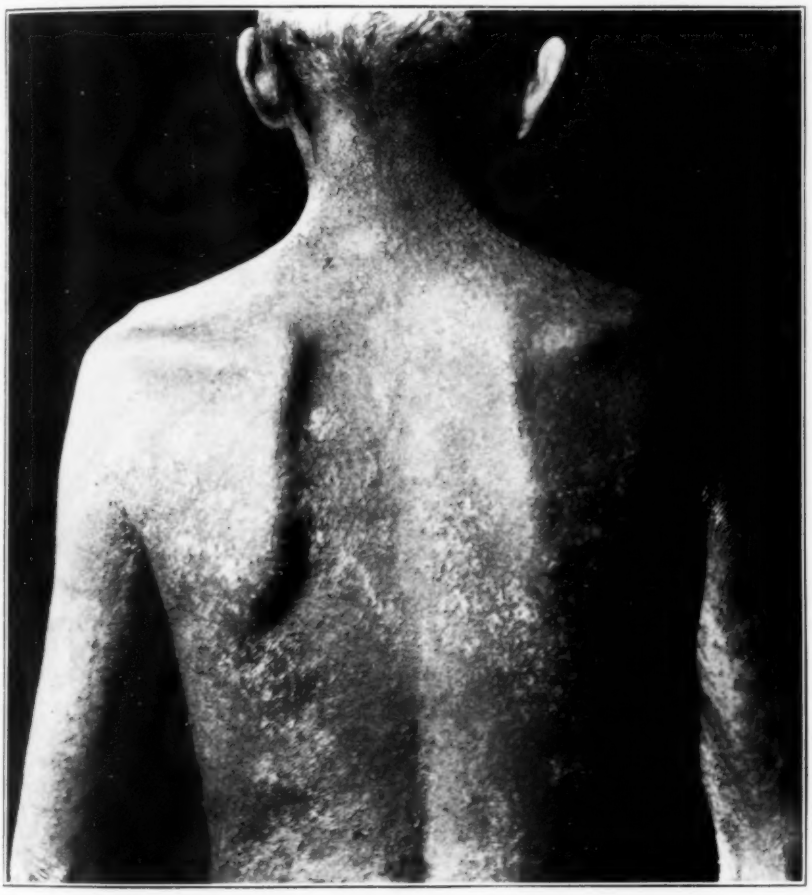

Fig. 6.—Posterior aspect of neck, back and arms.

descriptive purposes only, and do not signify separate disease entities. They offer a means of conveying a fairly accurate idea of the clinical picture under discussion, but it seems futile to carry on long academic dissertations as to why a given case belongs in one group or another.

If there were any essential difference between the various forms of ichthyosis, a microscopic examination of a piece of tissue should reveal it.

It is practically universally admitted that the essential abnormality is hyperkeratosis. This varies in a degree in different cases. Aside from this there are no characteristic pathologic changes. It is, therefore, not necessary to repeat here the descriptions of microscopic examinations of tissue in the various forms of ichthyosis.

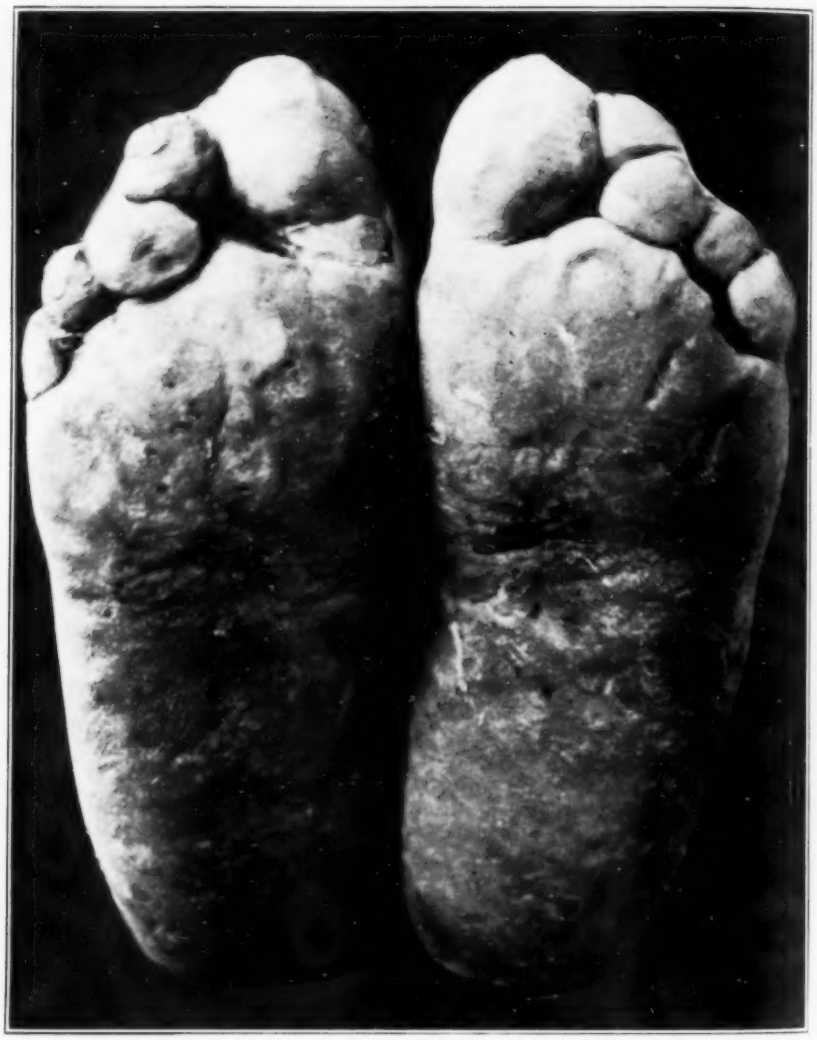

Fig. 7.—The soles after roentgen-ray treatment.

MacKee and Rosen's [12] summary of the histologic findings in cases of ichthyosiform erythroderma would answer very well for the other

12. MacKee, G. M., and Rosen, Isadore: Erythrodermie congenitale ichthyosiforme, J. Cutan. Dis. **35**:235-252, 343-361, 511-540, 1917.

forms. Since it also represents a summary of a large group of cases reported by different authors and sheds some light, especially in connection with certain observations on a case reported in this paper, on the developmental mechanism of the bullae occasionally observed, I shall report this summary in full.

There is a pure hyperkeratosis which is usually quite adherent. The thickened horny layer may extend into the hair follicles for a considerable distance and it may even *involve the orifices of the sweat ducts.* The granular layer varies from complete absence to increased thickness, not only in individual cases, but in a

Fig. 8.—Palmar surface after roentgen-ray treatment.

single section from one case. The rete may be moderately acanthotic or it may depict varying degrees of compression and thinning, depending on its relation in respect to the papillae and probably also to the stage and particular characteristics of the affection and the part of the body from which the skin is removed. The rete hardly ever represents noteworthy features other than those just described. Occasionally a peculiar type of edema or dyskeratosis is encountered. The rete pegs may be flattened out or they may be enlarged and anastomosed. The papillae may be broad and flattened or they may be narrow and elongated. The surface of the epidermis is likely to be found undulating. There is usually

slight inflammation of the upper part of the derma. The capillaries are dilated and surrounded by a slight to moderate lymphocytic infiltration. The connective tissue is usually unaffected; it may be slightly edematous, thickened, thinned or slightly degenerated. The elastic tissue is likely to be slightly reduced and fragmented. The oil glands are usually normal, but they may be dilated or show evidence of degeneration. The orifices of the oil ducts are likely to be compressed. The sebaceous glands are usually unaffected.

Fig. 9.—Dorsa of hands after roentgen-ray treatment

Ichthyosis congenita might, then, according to much weighty evidence, be regarded as the most severe form of ichthyosis. Infants in whom the anomaly is most pronounced die soon after birth. Others will live, sometimes to a good age, but probably always handicapped by a somewhat stunted physique aside from the cutaneous disturbance. Ichthyosiform erythroderma still presents pronounced cutaneous changes and also other physical defects, but is not incompatible with life and even the enjoyment of reasonably good health. Only with the severe forms are

the patients handicapped; with the milder forms they often are in as good condition as with the ordinary type of so-called ichthyosis vulgaris. In many instances it may be difficult, even for experienced observers, to classify them in any of those groups. The cases here reported, for instance, could be classified with Riecke's ichthyosis congenita tarda, Brocq's ichthyosiform erythroderma or Janovski's ichthyosis hystrix. Ichthyosiform erythroderma may thus be assumed to occupy an intermediate position between ichthyosis congenita and ichthyosis vulgaris. Ichthyosis vulgaris comprises the milder types of the disease, but in its pronounced form often constitutes a definite handicap as the result of the cutaneous anomaly, while the development is normal and the general health good, very likely because the cutaneous disturbance is not sufficiently severe to interfere with the normal functions of the body.

## COMMENT ON CASES

While the cases here reported presented several features of which I could find no specific mention in the literature, there was practically no doubt about the diagnosis. The ichthyotic features were pronounced. If we were to insist on a sharp division of the different forms of ichthyosis, it would seem justifiable to classify these cases as ichthyosiform erythroderma, in the conventional sense. So far as I can judge, the bullous lesions would help to place them in its subdivision, since such lesions are not a prominent part of the typical congenital or vulgaris types in the opinion of any authority. The pronounced hyperkeratosis should easily disarm the suspicion of a possible true epidermolysis bullosa. Yet Wile's [13] hint that the disorganization of the elastica, as observed in his cases of ichthyosiform erythroderma, suggests that a close relationship to epidermolysis bullosa is very plausible and worthy of further careful consideration. In the following case I believe there was evidence of a close relationship between these congenital defects.

A young man, aged 19, had had some cutaneous abnormality in the region of the navel at birth. At the age of 4 months, vesicles began to appear on the feet and had persisted more or less since. Soon after, the hands and face also became affected. The major portion of the skin was unusually smooth, and the hair, including that of the scalp, lacked proper development. The folds of the skin at the neck, the axillae and elbows were erythematous and scaly. The appearance of vesicles and pustules in this case seemed more related to trauma even of as mild a character as from the friction of shoes and bed linen.

Anomalies of the skin vary so much that it would be preposterous to draw a sharp dividing line between all cases of ichthyosis and epidermolysis. Lenglet and Jadassohn, in their classifications of dyskeratosis,

13. Wile, U. J.: Familial Study of Three Unusual Cases of Congenital Ichthyosiform Erythroderma, Arch. Dermat. & Syph. **10**:487-498 (Oct.) 1924.

evidently also have this conception. Our knowledge as to the underlying disturbance in these congenital anomalies is evidently still so imperfect that the dividing line cannot be drawn.

The formation of bullae was a pronounced feature in both of my cases, especially in case 1. On inspection it would seem justifiable to think of a possible epidermolysis bullosa, especially since in the second case the bullae were most abundant on the hands and feet and at times appeared to be precipitated by trauma. The traumatic factor, however, was negligible in case 1. A study of a section of the skin taken in case 1 showed that the elastica does suggest some variations from the normal. They are seemingly very slight and hardly amount to true disorganization. It may well be that the cutis shares to a moderate degree in the developmental aberration and that the type of manifestation is dependent to a large extent on the severity and amount of tissue aberration seen in these cases, and that the great variety of pictures is largely due to the degree of abnormal function or structure manifested by the cells in either the derma or the epidermis.

In case 1 the most striking feature was the development of enormous numbers of bullae practically everywhere whenever the patient became heated. Apparently the bullae appeared at about the time when the normal perspiration becomes visible. Exercise, warm baths and even an unusually hot day always brought on an exacerbation. It was impossible to escape the impression that the sweating process was definitely responsible for the bullae. Their development, therefore, seems akin in its mechanism to the formation of sudaminal vesicles. There was probably partial obstruction to the sweat duct and interference with the free egress of the sweat. MacKee and Rosen point out that in many cases of ichthyosiform erythroderma the thickened, horny layer may involve the orifices of the sweat duct to the extent of compressing them. It is likely, therefore, that just this particular degree of hyperkeratosis is necessary in these cases to produce the bullous lesions and that there need be no disturbance in the elastica or collagen, at least not to a degree sufficient to produce bullous lesions because of such a defect. Yet, on the other hand, in certain types of cases, for instance those reported by Wile, the disturbance in the connective tissue of the skin may be sufficient to allow the formation of bullae on the slightest traumatic provocation; in such cases the obstruction to the sweat ducts may be entirely absent. Thus in certain cases the abnormality in the epidermis may be responsible for the formation of bullae. In other cases it may be attributable largely to defects in the connective tissue bundles; in still other cases, there may be a mixture of these two factors.

Case 2 undoubtedly also belongs in the same group as the first. The formation of bullae as the result of overheating, however, was not so clear. Unfortunately, a microscopic study of the skin was not made.

The presence of bullae in greatest numbers about the hands and feet and their increase in number by pressure suggest that trauma was probably a factor. It is entirely possible, aside from the obstruction in the sweat ducts, that there may have been sufficient anomaly of the connective tissue bundles of the derma to have been at least partly responsible for the formation of bullae.

The most noteworthy feature of case 2, however, was the decided improvement produced by roentgenologic treatment. The bullae no longer appeared so readily after treatment. Since the bullous lesions were present in such large numbers on the hands and feet, the patient was practically bedridden. This of course reflected on his general health and vitality. Following the treatment, he was able to get around and was able to help with the farmwork, and his health improved. While occasional bullous lesions appeared, they were no longer nearly so troublesome as before treatment.

I shall not attempt to theorize about the rationale of the roentgenologic treatment. I believe, however, that such treatment may be decidedly beneficial; it is worthy of further trial in selected cases with congenital bullous lesions. Unfiltered roentgen-ray treatment was given in the spring of 1921. The dose was one-fourth skin unit, according to the method of MacKee, at weekly intervals for three doses. In July, 1925, three more doses of one-half skin unit each were given at weekly intervals.

## CONCLUSIONS

A study of the literature offers very little evidence to prove that ichthyosis congenita, ichthyosiform erythroderma and ichthyosis vulgaris are genetically different entities; they probably represent different degrees of severity of the same developmental anomaly. For practical, and especially descriptive, purposes, it is probably desirable to retain this classification.

Case 1 points strongly to a sudaminal mechanism in the production of bullae in certain types of ichthyosiform erythroderma rather than to some disturbance in the fibrilla of the cutis.

Case 2 shows that roentgenologic treatment may prevent, to a large extent, the development of bullous lesions in certain types of ichthyosiform erythroderma and thus materially benefit the patient.

Observation of my two cases and a digest of the literature suggest that bullae may be produced in ichthyosis by one of three mechanisms: by obstruction of the sweat ducts, developmental disorganization of the fibrillae of the cutis and a combination of these two factors.

## DISCUSSION

Dr. Udo J. Wile, Ann Arbor, Mich.: There are two points in Dr. Goeckerman's paper which I believe are deserving of discussion. One point to which he called attention is the close similarity between certain of these cases of ichthyosi-

form erythroderma and epidermolysis bullosa. In cases of the two diseases that have existed for a long time it becomes difficult at times to distinguish them, especially in the cases of ichthyosiform erytheroderma in which bullae occur. A great deal of atrophy occurs in both, the nails are usually involved and the differential diagnosis is difficult.

However, I believe a much more important phase of this subject did not find a place in the essayist's paper, and I believe it deserving of earnest study on the part of dermatologists. I refer to the distinct familial tendency of this disease, and to the fact that this particular form of dystrophy belongs to the group of so-called "recessive hereditary characteristics." The question of heredity in congenital anomalies of the skin has received little attention from us, but has received a considerable degree of attention from the students of heredity and genetics. It is important to show that the various forms of ichthyosis of such conditions as albinism and other forms of congenital dystrophies are transmitted to children, as are other normal characteristics. For this reason, I take exception to the statement of the essayist when he says that he believes ichthyosiform erythroderma and ichthyosis are genetically alike. The evidence seems to be that true ichthyosis is more often a direct hereditary transmitted trait, and ichthyosiform erythroderma is transmitted as a recessive hereditary characteristic.

A father who has ichthyosis is likely to transmit this to certain of his children without regard to the condition of the skin of their mother. This is not true of ichthyosiform erythroderma. In Dr. Goerckerman's case and in the ones I described about two years ago, the transmission was made more likely by the factor of consanguineous marriage. A case survey of the family history in this type of case is, I believe, the most important thing in the study of the genesis of the disease.

Dr. Frank W. Cregor, Indianapolis, Ind.: It seems to me that Dr. Wile has expressed my reaction to this paper; however, he has done so in different language from what I shall use. The well established familial character of both ichthyosis and epidermolysis bullosa will establish their hereditary character, and I wonder whether we have not in this case an ichthyosis plus an epidermolysis bullosa.

Dr. William H. D. Goeckerman, Rochester, Minn.: I fully agree with Dr. Wile that these cases merit further study, especially from the standpoint of heredity. I had three objects in presenting the paper: First, to call attention to the great variety of clinical pictures one sees in these ectodermal dyskeratotic or dysgenetic groups of cases. Often these cases elicit much discussion in medical meetings, or no discussion at all, because they are so bizarre and unusual that no one has seen anything similar, and yet if they are carefully analyzed one can only feel that they belong in one of these groups. The main object in presenting the first patient was to show that in the production of these bullous lesions the sweat glands may be the important factor, while in other cases some other factor may be operative. The third object was to show that we had obtained a striking result from roentgenotherapy. How to explain this I do not know, but in my second case it was effective.

# CONGENITAL PARTIAL ALBINISM

V. PARDO-CASTELLO, M.D.
HAVANA, CUBA

Congenital leukoderma is described in all textbooks under the name of partial albinism. The condition consists of achromic patches, irregularly distributed and often symmetrically situated. These patches are milky white, closely resembling those of vitiligo. Congenital leukoderma differs from vitiligo in being present at birth, in being hereditary with approximately the same distribution in all subjects of the same family, in the absence of peripheral pigmentation and in being fixed, neither growing nor diminishing in size in later years.

The cases reported were seen through the courtesy of Dr. J. A. Tremols of Havana. The patients were a mother and three children, 32, 4, 3 years and 8 months of age, respectively, all white, from direct Spanish ancestors, the possibility of any admixture of colored blood being carefully excluded. All of them presented extensive achromic patches over the chest, abdomen, legs and arms, of similar size and shape. In the first and second children, several islets of pigment were irregularly distributed over the achromic patches. In the legs the leukoderma was irregular, alternating with pigmented spots, giving a mottled effect like a leopard skin. In no place was there any increase in pigment, there being only two shades of color, that of the normal skin of the brunette type and the milky white of the leukodermic areas. On the center of the forehead and adjacent part of the scalp, there was in all subjects a triangular shaped leukodermic area on which the hair was white, contrasting sharply with the light chestnut color of the rest of the hair (poliosis circumscripta), figures 1, 2, and 3.

The patients were all in good general health, the skin being normal in every respect except for the lack of pigment.

The history of the condition could be traced back to the maternal great grandmother, through the grandfather and mother, to the three children, all with about the same distribution. There was no predilection for either sex, there being five females and six males affected in four generations. Of the sixteen members of the family in these four generations only five were free from the blemish (fig. 4).

## ETIOLOGY

The etiology of the condition is unknown. Consanguinity of the parents—which did not exist in these subjects—and nervous shock during pregnancy have been incriminated. Sometimes the achromic patches are in the form of bands corresponding to the distribution of the peripheral nerves. Sometimes pigmented nevi are present, alternating with the achromic bands.

Fig. 1.—Mother and child. Note achromic area and poliosis of the forehead.

Fig. 2.—Brothers. Note similar distribution and shape of achromatic patches.

Fig. 3.—Same child as in figure 2, showing irregular distribution of pigment on the back of the legs and arms; leopard skin.

Lesser [1] reported a case in which the congenital leukodermic patches were situated along the distribution of the hypogastric and cutaneous nerves of the neck. According to Riecke [2] congenital leukoderma may be unilateral.

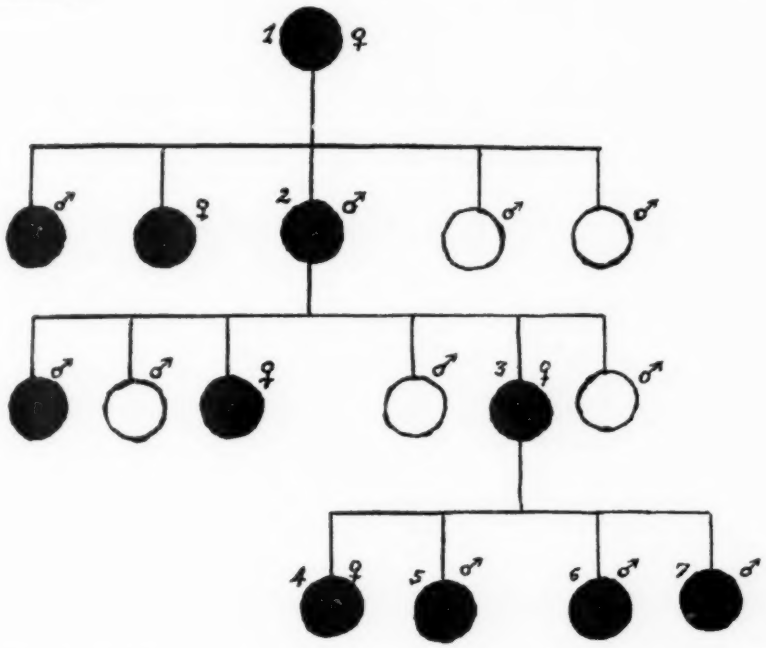


Fig. 4.—Family tree; *1*, great grandmother; *2*, grandfather; *3*, mother; *4*, *5*, *6* and *7*, grandchildren; *1*, *2* and *4* deceased. The black circles indicate persons with congenital leukoderma; white circles, normal persons.

I feel inclined to believe with Darier [3] and others that these cases of congenital leukoderma, improperly called partial albinism, are in reality cases of achromic nevi.

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1. Lesser, E.: Tratado de Enfermedades de la Piel y Venereas, Spanish transl., 1916, p. 195.

2. Riecke, E.: Tratado de las Enfermedades Cutáneas y Venereas. Span. transl., 1922, p. 454.

3. Darier: Precis de dermatologie, 1918, p. 349.

# XLVIII.—RECKLINGHAUSEN'S NEUROFIBROMATOSIS AND THE SKELETON

## A PLEA FOR COMPLETE STUDY OF THE DISEASE *

EDWIN P. LEHMAN, M.D.
Asistant Professor of Clinical Surgery, Washington University School of Medicine
ST. LOUIS

Brooks and Lehman in 1924 reported seven cases of Recklinghausen's neurofibromatosis [1] in which marked changes in the bones were observed. This material was published in a surgical periodical and probably did not become known generally among dermatologists. At least, recent dermatologic papers on Recklinghausen's disease attach no significance to these interesting and probably fundamental manifestations. For that reason, the following report of two additional cases is presented.

Bone changes found in association with Recklinghausen's neurofibromatosis have been noted here and there throughout the rich literature of the disease. No attempt to classify them or to define them as expressions of this complex disease comparable to skin and visceral expressions had been made previous to our report, with the exception of the observation of the common occurrence of scoliosis by Engman and Weiss.[2]

Three types of bone change were described by us: (1) scoliosis; (2) abnormalities of growth of individual bones; (3) irregularity of outline of bones ranging from central and subperiosteal cysts to pedunculated subperiosteal tumors. In interpreting these observations the following paragraphs may be quoted. Opinion in regard to this interpretation has not changed with increased experience.

> All of the bone changes which we have observed can be explained on the basis of the involvement of the bone by the growth of the tumor tissue which is characteristic of Recklinghausen's disease. With the development of a neurofibroma of a nerve in the periosteum, there is set up a certain amount of reaction, and bone destruction and regeneration follow. If, in the process of the development of the tumor, the osteogenetic element of the periosteum

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* From the Department of Surgery, Washington University School of Medicine, St. Louis. (Published as one of a series of Studies, Observations and Reports from the Dermatological Departments of that university and the Barnard Free Skin and Cancer Hospital, services of Drs. M. F. Engman and W. H. Mook.)

1. Brooks and Lehman: The Bone Changes in Recklinghausen's Neurofibromatosis, Surg., Gynec. & Obst. **38**:587, 1924.

2. Weiss: Curvature of the Spine in von Recklinghausen's Disease, Arch. Dermat. & Syph. **3**:144 (Feb.) 1921.

comes to cover over the tumor, then a thin shell of bone is formed over it and thus the X-ray appearance of a subperiosteal bone cyst is produced. If the tumor growth further involves the substance of the shaft of the bone and, particularly, if the growth of the neurofibroma is associated with a hyperplastic change in the lymphatics, then the entire bone is rendered more porous and more plastic. In the process of growth, this results in a growth in length of the bone, which is distributed throughout the entire bone instead of being confined to the region of the epiphyseal cartilages, and an abnormally long bone results. If the growth of tumor tissue is so placed as to destroy the epiphyseal cartilages, then the result may be an abnormally short bone. The entire process may be compared to osteomyelitis. If the infection is limited to the shaft and persists for a long period during childhood, the length of the bone may be abnormally great. If the infection destroys the epiphyseal cartilage, the bone is abnormally short. This abnormal softening of the bones by invasion of the tumor growth could also explain the scoliosis. The fact that scoliosis is so universally associated with the disease would be explained on the basis that the vertebrae are closely associated with the peripheral nerves. It is to be emphasized, however, that scoliosis may at least in part be due to asymmetrical growth disturbances of the lower extremities.

These observations emphasize the fact pointed out by Gould that Recklinghausen's neurofibromatosis is a condition affecting bone as well as skin and nerve. The fundamental process in the disease is one of tumor growth. It has long been known that the result of this tumor growth is to produce characteristic clinical manifestations in the skin and nerves. These observations indicate that equally characteristic clinical manifestations develop in the bones. The recognition of these changes in the bones is of diagnostic importance, particularly in those instances in which the complete clinical picture, heretofore considered classical, is not developed.[1]

The apparent fact that these observations have escaped the attention of essayists on the disease may be substantiated by reference to a number of recent discussions in the dermatologic literature. Louste, Caillau and Darquier [3] present a case of combined Recklinghausen's neurofibromatosis and acromegaly. The presence of scoliosis is mentioned only incidentally. Gravogna [4] reports a case of neurofibromatosis in which apparently no bone lesions were sought. Schneiderman [5] reports two cases of the disease. In both of these, bony asymmetry of the face is described in the general physical examination, but no understanding of the possible relationship of this finding to the disease or of its possible value in diagnosis, is evidenced. Wise and Eller [6] report two incomplete cases. In one of these, they express certain doubts as to the

3. Louste, Caillau and Darquier: Syndrome de Recklinghausen et acromegalie, Bull. Soc. franç. de dermat. et syph., February, 1925, p. 54.

4. Gravogna: Sur un cas de maladie de Recklinghausen, Ann. de dermat. et syph. **6**:610, 1925.

5. Schneiderman: Recklinghausen's Disease, Arch. Dermat. & Syph. **12**:483 (Oct.) 1925.

6. Wise and Eller: Recklinghausen's Disease Without Tumor Formation, J. A. M. A. **86**:86, 1926.

diagnosis, basing it finally on the presence of the full-blown disease in the parent. This same patient was operated on for scoliosis. Of this fact only incidental mention is made, whereas it is of extremely great confirmatory weight in the diagnosis.

Case reports follow of the two additional instances of skeletal changes, supplementary to the seven cases previously published. (For the sake of convenience these two cases have been numbered 8 and 9.)

Fig. 1 (case 8).—Elephantiasis of right thigh and leg and scattered subcutaneous tumors. The asymmetry of the pelvis is not clear because of the bent right knee. Pigmentation is barely visible.

## REPORT OF CASES

CASE 8.—M. E. V. (figs. 1 to 5), a white woman, aged 30, married, entered the Barnes Hospital in February, 1926. The family history and past history

were negative. There was no family history of multiple tumors or pigmentation. The presenting symptom at entrance was difficult urination and pain on urination. She could pass only a few drops of urine at a time. Lumps in and under the skin were first noticed at the age of 7 years, particularly on the right thigh and leg. These have been growing slowly since. Several of them have been removed surgically from time to time. They are not painful with the exception of a lump on the abdomen. The patient has had three pregnancies. The first was a difficult labor with forceps delivery. The second and third were cesarean sections which were undertaken for masses obstructing the pelvic outlet. The last cesarean section was performed in Barnes Hospital in 1919. The record shows that in addition to a mass impinging on the vagina, the diagnosis of slight general contraction of the pelvis was made.

Fig. 2 (case 8).—Note greater size of right innominate bone. Crest of ilium is considerably above limit of film on right and below it on left. Right pubic bone is displaced downward in relation to the left. A greater thickness of the head and neck of the right femur is possibly present as compared to the left.

Examination revealed a moderately nourished woman who presented a few scattered small fibromata mollusca over the body (fig. 1). There was considerable coffee-colored, pale pigmentation, especially about the pelvis, of too light a color to show in the photograph. The skin also showed numerous characteristic small bluish flecks of color overlying minute subcutaneous nodules. There was a marked elephantiasis of the right thigh and leg. When the

patient stood, there was a definite tilting of the pelvis upward on the right and a slight lumbodorsal scoliosis. When the patient sat squarely on a hard surface, the iliac crest on the right was 3 to 4 cm. higher than on the left. Measurements showed that there was lengthening of the right lower extremity in or below the pelvic girdle. This lengthening measured about 3 cm.

Fig. 3 (case 8).—Anteroposterior view of left ankle, showing subperiosteal cyst of tibia and resorption of fibula.

All over the body there were subcutaneous masses varying in size from those just palpable to discrete masses 10 cm. in diameter. In addition, there were much larger, diffuse masses which were soft, doughy and contained numerous small hard nodules. The tumor distribution was most profuse in the right thigh and leg and over the left part of the thorax and abdomen. Several strings of small nodules in the left side of the thorax corresponded

roughly to the course of intercostal nerves. A large, doughy, nodular mass on the anterolateral aspect of the right thigh corresponded accurately with the distribution of the external cutaneous nerve. (This manifestation was almost identical with the tumor mass described in case 1 in the previous report). The large tumor on the anterior abdominal wall shown in the photograph was the only tender tumor found. There was a large mass in the adductor region of the right thigh which was continuous with a mass partly filling the true pelvis. This mass could be felt to be firm, rounded, fixed, with nodular irregularities. The vagina was narrowed and elongated. The cervix was displaced to the left and situated extremely high up. Cystoscopic examination by Dr. John R. Caulk showed enormous elevation of the bladder due to outside pressure, with congestion of the mucosa. The eye-piece of the cystoscope pointed almost directly upward in entering the bladder. Rectal examination with the

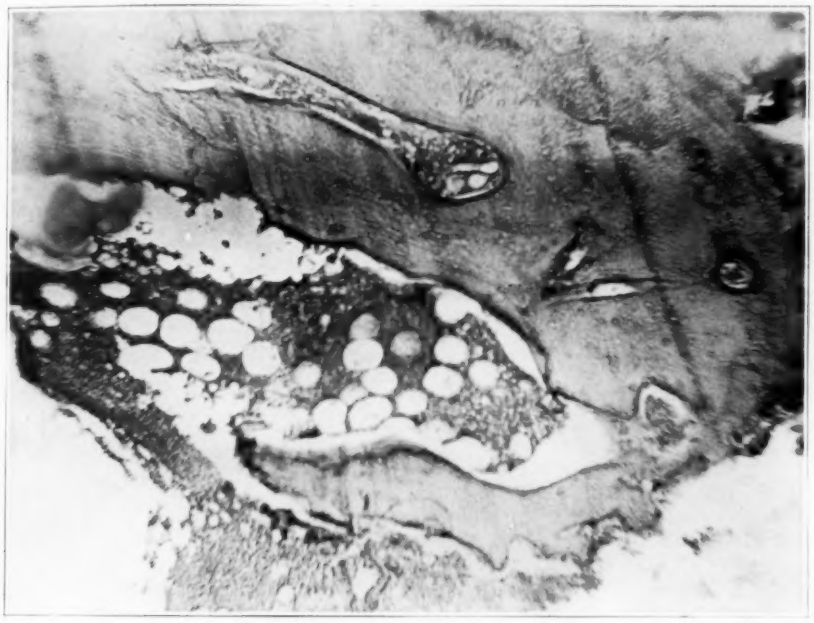


Fig. 4 (case 8).—Section of hypertrophied right ilium. Periosteal surface is at top of section. Note enlarged haversian canals and thin cortex.

finger disclosed the masses felt by the vagina. Proctoscopic examination was negative. A barium enema showed displacement and compression of the rectum by a tumor outside the bowel.

The urine showed a few white cells and a trace of albumin on admission. It was negative on discharge. The blood picture was entirely normal except for cells in the smear that resembled myelocytes. The blood Wassermann test was negative.

Bone Changes: (1) There was slight lower dorsal scoliosis probably compensatory to asymmetry of the pelvic girdle. (2) The right innominate bone was symmetrically enlarged (fig. 2). (3) The femur and tibia of the right leg were probably slightly longer than those of the left. (4) In the lower

third of the left tibia on the external aspect was a cystlike projection from the bone showing the characteristic covering with cortical bone that we have seen in earlier cases (fig. 3). This measured about 2 cm. in diameter at the base by 1.5 cm. in height. It had impinged on the fibula causing marked resorption of that bone.

On March 8, 1926, the pelvic tumor was attacked in order to relieve the symptoms of urinary obstruction. Exposure was made extraperitoneally by an incision above Poupart's ligament. A double handful of tumor tissue was scooped out from beneath the levator ani muscle. This tissue was characteristic of neurofibroma consisting of multiple nodules connected by fine strands. On cross-section they showed pearly white, glistening homogeneous structure. Microscopic examination showed typical neurofibroma. The patient suffered

Fig. 5 (case 8).—From a second area of the right ilium. The periosteal surface is above. Note penetration of cortex by cellular tissue (neurofibroma?), large haversian space (to right), thinness of cortex and area of calcium deficiency (*A*).

considerable reaction from the operation but gradually improved and was discharged seventeen days later with marked symptomatic improvement and definite relief of pressure about the bladder neck.

During the exposure at operation, a wedge of bone 2 by 1 cm. in size was removed from the enlarged innominate bone near the anterior superior spine. This bone cut with considerable ease, and the cortex appeared very thin. Microscopic examination (figs. 4 and 5) showed marked osteoporosis with large haversian spaces and a thin cortex. At one point there was complete penetration of the cortex by cellular tissue. The cortex and trabeculae in areas showed alterations in staining reaction suggesting deficiency of calcium.

Fibromatous tissue could not be demonstrated within the bone. However, the decalcifying process in the course of preparation of the specimen was probably carried on too long; as a result, the staining was inadequate and one could not say that fibroma was not present. The tuft of cellular tissue projecting through the cortex might easily be invading neurofibroma.

Case 9.—V. A. G. (fig. 6), a white woman, aged 38, married, entered Barnes Hospital in March, 1926, and was referred to me by Dr. M. F. Engman. The family history was negative in regard to multiple tumors. The past history showed many illnesses and poor general health. The patient had had an oophorectomy ten years ago. She had had considerable headache in recent years. She first noticed a nodule in the skin over the right clavicle five years ago. This

Fig 6 (case 9).—Lateral view of skull showing alteration of bone structure and cystic areas in bones of vault.

was excised by a surgeon and called a mole. Ten months later she noticed other nodules. At about the same time she noticed that her right eye was smaller than her left.

Examination revealed a well nourished woman of average stature without asymmetry of the skeleton. Over the right side of the neck from the lobe of the ear to the clavicle were scattered characteristic fibromata mollusca of a maximum diameter of 1 cm. The distribution here was limited to the

skin area of the cervical plexus. It did not cross the median line. The skin in this region appeared slightly darker than elsewhere on the body. There were sparse scattered telangiectases, pigmented moles and brownish pigmented spots over the body. There was one fibroma molluscum in the right upper arm. There was a paralysis of the cervical sympathetic nerve on the right, as shown by ptosis, narrowing of the pupil, and absence of sweating (Horner's syndrome). The laboratory examination was entirely negative. The ophthalmoscopic, lumbar puncture and blood Wassermann tests were negative.

Several fibromata mollusca were excised. Microscopic examination of this tissue showed neurofibroma.

Bone changes: 1. There was slight scoliosis in the cervicodorsal region. 2. The bones of the skull showed obscuration of the normal diploeic markings (fig. 6). The bone showed a coarsely granular texture. In the right parietal bone there were several irregular rarified areas with serrated margins in which all bone structure was lacking. The largest of these measured about 2 cm. in diameter. No external manifestations of these cranial findings could be detected.

COMMENT

These two cases add somewhat to our knowledge of bone changes in Recklinghausen's disease. In the first place, we see (case 8) overgrowth of a flat bone. All earlier instances of overgrowth of single bones were of long bones. Second, we can here study (case 9) the reaction of the bones of the skull to the disease. In addition, we have examples of unsuspected bone involvement detected only by complete roentgenographic examination (periosteal cyst in case 8, skull changes in case 9).

Of case 9, it may be said further that the findings of scoliosis and of cystic areas in the skull are of great diagnostic importance. Here we have an extremely early case with almost no pigment, with tumor involvement of only two sites, namely, the cervical plexus and possibly the cervical sympathetic chain. Is this Recklinghausen's disease? May one expect further gradual development into the full-blown characteristic picture? Certainly, on the basis of previous experience with bone manifestations of the disease, one can throw into the diagnostic balance these skeletal abnormalities of the patient. The value of a more thorough knowledge of such abnormalities could not be illustrated better.

By the microscopic study of the specimen of hypertrophied innominate bone removed at operation in case 8, it was hoped that light might be thrown on the cause of the hypertrophy. Certainly, part of the hypothesis presented in the paragraphs quoted above is substantiated, namely, that these hypertrophied bones are softer than normal, that they are in a plastic state favorable for interstitial growth. The hard bone is markedly diminished in quantity, and, in places, calcium deficiency is suggested. The bone cut with great ease at operation. The point in the hypothesis that is unsubstantiated is the cause of this osteoporosis. Is it due to infiltration of the bone with tumor tissue? The question cannot be answered from this material. The tissue does not make an affirmative

answer impossible; in fact, the area shown in the microphotograph where the cortex is penetrated by soft tissue is at least suggestive of such an answer.

An advance in our knowledge of this bizarre disease can be made possible by observation of all cases for bone lesions. In every case, complete or incomplete, proved or merely suspected, there should be a roentgenographic investigation of the entire skeleton. A study of a case of Recklinghausen's disease should not be considered complete without such investigation. When material has been collected in sufficient quantity to warrant generalization, the conclusions that we drew in our original paper, and that I repeat here, may be considered false. Until that time, those conclusions should be used in visualizing the complete picture of the disease. Blindness to any repeated manifestation of a pathologic process will not advance knowledge. There is no doubt that Recklinghausen's disease attacks bone as well as soft tissues. Information concerning the manifold variations of this attack is badly needed. The dermatologists, who see many more cases than do the internists or the surgeons, are the logical sources of this information.

# Obituary

## EDWARD BENNETT BRONSON, M.D.

1843-1925

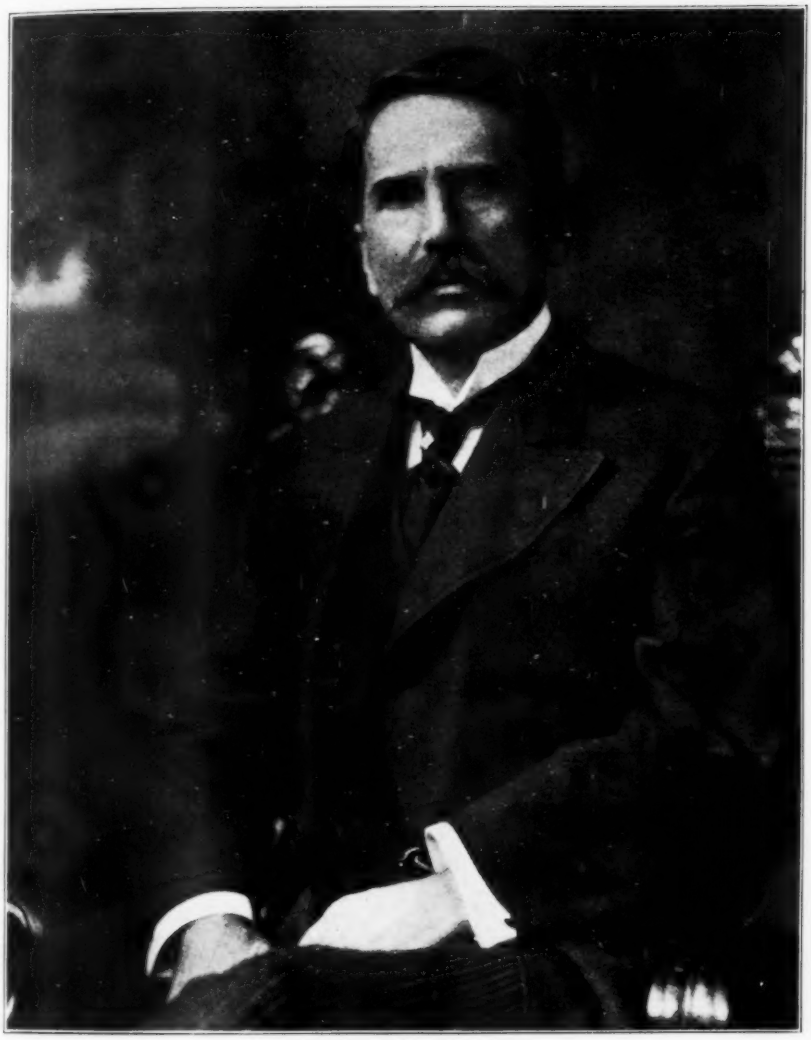
Another pioneer of American dermatology has gone from us, and his sudden and tragic death is deeply regretted by all who knew him. On the night of November 18, a fire occurred in his home, and by the time assistance arrived he had been asphyxiated.

Dr. Edward Bennett Bronson, son of the Rev. Thomas and Cynthia (Bartlett) Bronson, was born on June 12, 1843, in Hartford, Conn. His preliminary education was obtained at the Ellington School for Boys and Hartford Grammar School. In 1865, he graduated from Yale University, receiving the degree of A.B. After graduation he studied for six months in the Yale Medical School and then entered the College of Physicians and Surgeons of New York, from which he received the degree of M.D. in 1869. After serving as intern in Bellevue Hospital and spending three years abroad in medical study, he began the practice of medicine in New York City.

In his earlier days, Dr. Bronson was attending physician to the Northern, the New York and the Outdoor Bellevue dispensaries; assistant surgeon to the New York Eye and Ear Infirmary, visiting physician to the House of Mercy of New York and pathologist to the Metropolitan Throat Hospital. He served for many years as visiting physician to the City Hospital, becoming later a consultant to that hospital and to the Babies' Hospital.

Dr. Bronson was clinical professor in the Woman's Medical College and professor of dermatology in the New York Polyclinic Medical School and Hospital from 1882 to 1904, when he was made professor emeritus. He was for many years an active and later an honorary member of the New York Dermatological Association and president of the latter in 1891-1892. He was also a member of the New York Academy of Medicine, the New York County Medical Society, the Harvey and American Therapeutic societies.

Dr. Bronson's literary contributions, while not numerous, were scholarly and frequently of a philosophic type. One of his best medical articles was one on "The Sensation of Itching," written in 1890 and published three years later in "Selected Monographs on Dermatology" of the New Sydenham Society. Among his excellent publications were articles relating to the classification of skin diseases. His scholarly



EDWARD BENNETT BRONSON, M.D.

1843-1925

attainments were shown by his being one of the translators of Ziemssen's "Cyclopaedia of the Practice of Medicine" and an associate editor of Foster's "Encyclopedic Medical Dictionary" (published in 1888-1894.) He was also a member of the editorial staff of the *Medical Record* and one of the collaborators of the *Archives of Dermatology,* 1875-1877.

Dr. Bronson was modest and dignified, a man of high ideals and principles. He had always enjoyed good health, and with his black hair and erect carriage was unusually young looking. He was fond of outdoor exercise and a lover of music. In his later years he had largely retired from active practice and devoted much of his time to reading and study. He was a member of the University, Century and Quill clubs, and was unmarried.

Dr. Bronson was admired and beloved by all who knew him. His loyalty to his friends and his endeavors to uphold the best traditions of the medical profession were unquestioned. Those who knew him will always think of him as one who possessed in a preeminent degree the qualities which characterize the scholar and the gentleman.

HOWARD FOX.

# News and Comment

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Wesley T. Lee, Sec., 220 Clarendon St., Boston.

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CINCINNATI DERMATOLOGICAL SOCIETY

August Ravogli, Pres., Doctors' Bldg., Cincinnati.

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La Société Française de Dermatologie et de Syphiligraphie.

Section on Dermatology, Royal Society of Medicine.

British Association of Dermatology and Syphilis.

Berlin Dermatological Society.

Cologne Dermatological Society.

German Dermatological Society in Czechoslovakia Republic.

Vienna Dermatological Society.

Munich Dermatological Society.

Deutsche Dermatologische Gesellschaft.

# Abstracts from Current Literature

ERYSIPELAS: OBSERVATIONS ON THE ETIOLOGY AND TREATMENT WITH ERYSIPELAS ANTISTREPTOCOCCIC SERUM. K. E. BIRKHAUG, J. A. M. A. **86**:1411 (May 8) 1926.

The author's investigations have demonstrated that a specific type of *Streptococcus hemolyticus* is the causative agent of this disease.

A serum against this organism was produced and given clinical trial in sixty cases of erysipelas. Prompt benefit was obtained when the serum was administered within the first three days of the disease; when used later, the result has been excellent, but larger doses and repetition of the injections were often necessary. A skin test was devised which was used to determine the adequacy of the dose.

The serum was not refined, and some annoying instances of serum sickness occurred. It is hoped that these will be eliminated by the use of a refined globulin serum.

GENERALIZED ALOPECIA. G. WILSON and N. W. WINKELMAN, J. A. M. A. **86**:1424 (May 8) 1926.

The authors record two cases of this condition associated with endocrinologic disturbances. In a third case no abnormalities were noted.

In the first patient, a woman, a complete hysterectomy had been performed one year before the onset of the alopecia. She died from a tumor of the brain. The second patient had been under severe emotional strain during the late war, but showed no abnormalities besides the alopecia.

In the last two cases, pluriglandular therapy was a failure.

LEUKODERMA SYPHILITICUM. BEDFORD SHELMIRE and T. J. CALHOUN, J. A. M. A. **86**:1428 (May 8) 1926.

This article contains a report of two cases of generalized leukoderma which followed a macular syphilid in each instance. The authors were able to satisfy themselves that the depigmentation occurred at the sites of former macules. Repigmentation occurred but apparently not as an effect of antisyphilitic therapy.

THE TREATMENT OF DEEP ROENTGEN-RAY BURNS BY EXCISION AND TISSUE SHIFTING. J. S. DAVIS, J. A. M. A. **86**:1432 (May 8) 1926.

Davis believes that the best treatment for deep roentgen-ray burns is by complete excision, tissue shifting and skin grafting. Though he has seen many cases in which ultraviolet light has been tried, in none has the slightest benefit been obtained, and, as a matter of fact, he believes that ultraviolet light treatment is harmful in chronic radiodermatitis.

The results of the surgical procedure advocated have been gratifying. Pain is relieved and often function restored.

SPOROTRICHOSIS: REPORT OF TWO CASES. R. M. CARTER, J. A. M. A. **86**:1751 (June 5) 1926.

Two cases of the disease, both originating in Wisconsin, are reported. In each case, the disease followed a trivial injury to the hand, which was succeeded

by the common nodulolymphangitic type. The patients were cured with potassium iodide. *Sporotrichum schenkii* was obtained by culture from both cases.

[The author mentions that only two previous cases are recorded from Wisconsin, but he evidently overlooked the article of H. R. Foerster, Am. J. M. Sc. **167**:54 (Jan.) 1924, in which five cases originating in that State are reported.]

TYPES OF NEUROSYPHILIS IN RELATION TO TREATMENT. H. A. BUNKER, JR., J. A. M. A. **86**:1815 (June 12) 1926.

In view of the recent advances in the treatment of neurosyphilis, it becomes of great importance to determine the proper therapeutic attack for each case. It is of less importance to know whether a patient has a meningovascular or parenchymatous form of the disease than to determine the progress that he has made under a particular form of therapy.

The response of a patient with neurosyphilis should be gaged by repeated spinal fluid examinations. Improvement in symptoms is not the true index of a favorable effect of therapy. If the patient is showing no improvement in the spinal fluid tests, he should be given another form of treatment. From the practical standpoint, the author suggests a minimum of twelve injections of arsphenamine, then a spinal fluid examination. If improvement is not noted, malaria treatment is suggested as time conserving and therapeutically more effective than other specialized forms of neurosyphilitic treatment.

In any event, if a particular form of treatment does not prove beneficial in a given case, it should be discarded and another method tried.

ARACHNIDISM: A STUDY IN SPIDER POISONING. E. BOGEN, J. A. M. A. **86**:1894 (June 19) 1926.

Bogen has found reports of 150 cases of spider bite poisoning in the United States, and records an experience of fifteen more cases seen in the General Hospital at Los Angeles. The spider that produces the poisonous effects is *Latrodectus mactans*. This is a black spider about half an inch long, with a red patch on the ventral surface.

Following the bite, there is severe pain, but no localized swelling. The pain radiates to nearby points, sometimes involving the whole body, and is cramping, throbbing or aching. In addition, there is profuse perspiration, restlessness, nausea and vomiting, dyspnea, vertigo and other symptoms. A few deaths are recorded.

Treatment has consisted of sedatives, stimulants and eliminative measures. As one bite appears to convey some degree of immunity, the author tried convalescent serum in four recent cases, with beneficial effect, especially when it was administered shortly after the bite occurred.

RADIUM APPLICATOR FOR TREATMENT OF LESIONS ABOUT THE HEAD, FACE AND NECK. W. H. KENNEDY, J. A. M. A. **86**:1907 (June 19) 1926.

The apparatus consists of a leather head-band, copper wire and universal ball joint made to be used with one-fourth inch rubber tubing, in which the radium is placed. It allows adjustment in any position and provides perfect contact with the lesion, or fixed distance application.

BLASTOMYCOSIS. C. M. HAMILTON, Southern M. J. **19**:431 (June) 1926.

The author records eight cases of the common dermal type of the disease. These cases illustrate the value of early diagnosis and perseverance in treatment. Treatment consisted in removal of the involved tissue, radiation and iodine medication, and this has proved satisfactory.

MICHAEL, Houston, Texas.

BOWEN'S DISEASE. P. L. BOSELLINI, Brit. J. Dermat. & Syph. **38**:47, 1926.

After discussing at length the clinical and pathologic features of various epithelial growths, Bosellini concludes that there exists a syndrome, described by Bowen and well individualized, like other epitheliomatous forms, to which belong different types of superficial epitheliomas, defined, owing to their clinical aspect, by the terms "pagetoid epithelioma," "erythematoid epithelioma," "sclerodermic epithelioma," "superficial rodent ulcer," "multiple basocellular epithelioma," etc., and the separation of which from the picture of Bowen's disease as anatomic and clinical entities is not yet sufficiently justified by the facts. On the contrary, all these anatomic and clinical appearances may be met with in the plaques of Bowen's dermatosis, especially if the latter is observed during the whole of its long evolution.

He then describes two cases of his own, one of which is of special interest as regards the relationship of Bowen's disease to nevoid conditions—the senile keratoses.

SENEAR, Chicago.

DERMATITIS SCROFULOSA. BARBER and DOWLING, Proc. Roy. Soc. Med. **19**:33 (May) 1926.

The authors presented a group of cases under the designation of dermatitis scrofulosa. The eruption occurred on the limbs and trunk rather than on the face; when it did occur on the face, the patches had no predilection for the skin around the mouth. They were not fissured, unless irritated by soap and water, and they had a characteristic tint which varied from a pinkish-fawn color to a dirty brownish hue. The scales were larger and more flaky and fairly easily detached; the patches were not as a rule, circular, but were oval or irregular, and at times formed large sheets, particularly below the margin of the hair on the temples and on the limbs. The authors thought that dermatitis scrofulosa corresponded to the eczematoid trichophytid described by Jadassohn and Guth, and that it was an eczematoid reaction produced by sensitization of the epidermis to tuberculin. The reproduction of the eruption by the application of tuberculin favored this view. An interesting point was the rapidity with which the lesions disappeared under the influence of ultraviolet light.

In discussion Dr. Whitfield questioned the possibility of a tuberculous origin for this group, although he thought that eczema scrofulosorum of Boeck and his (Whitfield's) discoid eczema were identical.

Dr. Adamson also thought the eruption was independent of tuberculosis.

CASE OF ACNE AGMINATA. H. C. SEMON. Proc. Roy. Soc. Med. **19**:46 (May) 1926.

The patient was a woman, aged 37, who had lesions consisting of raised, reddish-brown, waxy papules about the size of a hemp seed. They were grouped in clusters of from six to twelve on the chin, cheeks and scalp. There was no tendency to necrosis or suppuration. Diascopy revealed a definite fawn-colored infiltration. No scars were present. Adenoma of the sebaceous glands was suspected, but before excision of a papule for histologic examina-

tion, the patient was seen by Dr. Gray, who sent a considered opinion that this was probably a case of so-called acne agminata or folliclis, of tuberculous etiology, and allied to the papulonecrotic group of tuberculids. The histologic findings amply confirm this view, as could be seen in the slide submitted.

There was round cell infiltration in the cutis, with several tubercules containing giant cells and lymphoid with a few mast cells. Light treatment combined with sodium morrhuate injections had effected a distinct improvement.

In the discussion, Dr. Gray said that he had treated with sodium morrhuate injections a series of patients who had lupus vulgaris, a series who had lupus erythematosus and one or two who had known tuberculids, such as Bazin's disease, also two who had conditions belonging to the benign lymphogranulomatosus group. The effect on lupus vulgaris and lupus erythematosus had been very slight; the improvement which resulted in some cases might have occurred from other causes. But the effect in the first case of sarcoid was extraordinary; this patient had been treated with arsphenamine and many other remedies, with only slight transitory effect, but half a dozen injections of sodium morrhuate cleared up all the lesions, and the patient had remained well. Dr. Gray had now under treatment a patient with an extensive case of lupus pernio, who was also responding well to the treatment. He was anxious that the treatment should be tried for acne agminata, because he thought it might help to settle the nature of the condition. Members who tried it in these cases would report their results.

URTICARIA PIGMENTOSA IN AN ADULT. ERNEST MALLAM, Proc. Roy. Soc. Med. **19**:4 (May) 1926.

A woman, aged 43, married, had an eruption that first appeared when she was 41; it was situated on the arms — especially on the forearms and backs of the hands — the inner side of the legs, the dorsum of the feet, and, to a slight extent, on the trunk. As regards its main features, the case illustrates all the six characteristics enumerated by Dr. Hannay in his paper in the *British Journal of Dermatology and Syphilis* in January, 1925, as supposedly commoner in adult cases: (1) the urticaria is mild; (2) the lesions are small; (3) the eruption is macular; (4) it is not of the xanthalasmoid type; (5) the onset is after puberty; (6) mast cells are absent; although he proves that not any of these points is essential.

REPORTS OF THE KALA-AZAR COMMISSION 1924-25, Indian J. M. Res. (suppl. ser.) Memoir No. 4, February, 1926.

This 288 page supplementary number of the *Indian Journal of Medical Research* embodies the results of the first year's work of the commission recently constituted in India for the study of kala-azar. In it are also incorporated contributions from the Kala-Azar Ancillary Enquiry and one or two papers from other workers in India. Christophers, Shortt and Barraud record observations on the morphology and life cycle of the parasite of Indian kala-azar in culture. Starting as a mature flagellate the result of early development from the Leishman-Donovan body, a parasite leaves the group where it was formed and becomes a swimming form. This form eventually comes to rest either in some chosen situation or at some point beyond which it is unable to progress. It now divides and repeats this process until a considerable number of short multiplicative forms are produced, among which are some that develop into active forms with vibratile flagella and once more swim away to repeat the

cycle. Christophers and Shortt were able to grow *Herpetomonas donovani* on NNN medium between 16 and 34 C., growth, however, being better between 22 and 30 C. The same authors indicate that the parasite of kala-azar in the flagellate stage is fairly resistant to changes in osmotic pressure and will yield cultures in relatively low salt concentrations but is likely to be unable to withstand the action of water. Shortt and Swaminath produced a systemic infection of a monkey (*Macacus rhesus*) by intradermal inoculation of spleen pulp material from a case of kala-azar. Greig and Christophers duplicated this result following the introduction of infected material into the lumen of the small gut. Christophers, Shortt and Barraud obtained 84 per cent of positive infection in mice by intraperitoneal inoculations. Feeding cultures to mice was unsuccessful with one exception. Shortt and Swaminath examined 138 bedbugs caught in the bedding in cases of kala-azar. Cultures were uniformly negative. Christophers, Shortt and Barraud examining different species of culicoides that had fed on kala-azar patients found 25 per cent positive results with one variety only — (*Phlebotomus argentipes*). Knowles, Napier and Smith demonstrated *Herpetomonas donovani* in the foregut or midgut of this parasite under the foregoing circumstances. Christophers, Shortt and Barraud observed the life cycle in *Phlebotomus argentipes* to be the same as seen in cultures. Control examinations were negative. Feeding larvae on cultures of *Leishmania donovani* gave negative results. Articles on the bionomics, anatomy and methods of breeding of sand flies were presented. Napier's conclusions from an epidemiologic study are as follows: There is considerable evidence in favor of the hypothesis that man forms an essential link in the endless chain of kala-azar transmission, but the hypothesis is not proved. There is very strong evidence that the disease cannot be spread without the aid of an intermediate host, but again the case is not proved. The transmitter is probably a blood-feeding athropod, probably a member of either the genus *Phlebotomus* or the genus *Culicoides*. In the case of most of the arthropods suggested as possible transmitters of the disease there are numerous epidemiologic observations which negative the suggestions, but in the case of *Phlebotomus argentipes* every epidemiologic observation appears to be in keeping with the theory that that insect is the transmitter of the causative organism of kala-azar.

GUY, Pittsburgh.

A SECOND CASE OF PURPURIC AND PIGMENTED LICHENOID DERMATITIS. GOUGEROT and P. BLUM, Bull. Soc. franç. de dermat. et syph. **32**:433, 1925.

Situated on the left forearm, thigh and foot, and accompanied by slight telangiectasia, the lesions were suggestive of Schamberg's progressive pigmentary dermatosis. The patient, a woman, aged 31, had had the condition for eleven years, with no subjective symptoms.

TWO CASES OF TRICHOPHYTOSIS DUE TO A FAVIFORM TRICHOPHYTON. E. BODIN, Bull. Soc. franç. de dermat. et syph. **32**:435, 1925.

Suppurating patches on a baby's face, and an impetigo-like lesion on a woman's wrist were found to be due to infection with a faviform trichophyton, probably *Trichophyton album*. In both cases the infection was apparently of animal origin.

SYCOSIFORM CHANCRES OF THE CHIN AND OF THE MUCOUS SURFACE OF THE LOWER LIP. THIBAUT and MARIN, Bull. Soc. franç. de dermat. et syph. **32**:439, 1925.

There were two slightly infiltrated, crusted lesions with considerable enlargement of the regional lymph nodes. The dark-field examination was negative, but the Wassermann reaction was positive.

ULCERATING LEUKEMIC TUMOR OF THE FOREARM. LOUSTE, CAILLAU and LEROND, Bull. Soc. franç. de dermat. et syph. **32**:440, 1925.

In a woman, aged 52, there had been a transient erythematous eruption three years previously, followed in turn by enlargement of the lymph nodes and spleen and by an extensive ulceration of the forearm. The histologic findings are described.

CHANCRE OF THE BASE OF THE THUMB. LOUSTE, BRAUN and A. MARIN, Bull. Soc. franç. de dermat. et syph. **32**:444, 1925.

In an upholsterer, the lesion appeared at the site of an industrial injury. The epitrochlear lymph node was not palpable, but there was axillary involvement.

THREE CASES OF BISMUTH ABSCESS. J. GOUIN and ALLANIC, Bull. Soc. franç. de dermat. et syph. **32**:445, 1925.

Appearing from six weeks to three months after injections of bismuth hydroxide in oil, the gluteal tenderness was accompanied by malaise, nausea, vomiting and fever. The bismuth compound, and not the oil, was blamed. Incision and drainage was necessary.

LOCAL ACCIDENTS FOLLOWING INJECTIONS OF BISMUTH HYDROXIDE. LACAPERE and GALLIOT, Bull. Soc. franç. de dermat. et syph. **32**:449, 1925.

In a series of 9,000 injections of bismuth, the hydroxide was used in 90 per cent, and the complication occurred in twenty-two cases. In seventeen of these, a certain preparation of bismuth hydroxide had been used, which was found by its manufacturer to be faulty, the oil vehicle being blamed. According to this, it would seem that the use of bismuth hydroxide in general is no more dangerous than the use of the arsphenamines. PARKHURST, Toledo, O.

SCAR CARCINOMA. M. IWAMOTO, Mitt. ü. allg. Pathol. u. path. Anat. **2**:573 (April 18) 1926.

Thirteen cases of carcinoma in cutaneous scars were seen in Sugimura's clinic at Sendai, Japan, during the past seven years. In nine the scars resulted from extensive burns, in the others from injuries. The site was the lower extremity in six cases, the upper extremity in two, the head in five. The carcinoma developed during the so-called cancer age, but in most cases the scar had existed since childhood. The carcinoma appeared as an ulcer or fungous growth toward the center of the scar. Histologically, twelve of these cases were pavement epitheliomas with distinct cornification; one was a basal cell carcinoma. Iwamoto states that basal cell carcinoma has not before been reported in a scar. The tendency is to spread on the surface, but in four cases the tumor had invaded the underlying bone. Inflammatory swelling of the regional lymph glands was present in six cases, but no metastases were found. The patients' general health was little affected. In all cases the carcinoma was

preceded by repeated irritation of the scar or breaking open of an obstinate ulcer. Four patients are well from three to seven years after operation (amputation or simple removal of the tumor). One died of recurrence after amputation. Two were seen too late to benefit by treatment. The others have disappeared from observation or were operated on recently.

CARPENTER, Chicago.

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## DERMATOLOGIC ABSTRACTS

### THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

MECHANISM OF CANCER METASTASIS. M. T. BURROWS, Arch. Int. Med. **37**:453 (April) 1926.

Observations are reported on by Burrows from which it is evident that metastases in cancer are not the result of a simple migration of cancer cells from the cancer to distant organs. Metastases are primarily the result of the spread of a liquid substance from the main tumor mass. This substance spreads over surfaces. It is liberated through a digestion of cells in the center of the mass of cancerous tissue. This digestion is not an autolysis resulting from the absence of oxygen, but the result of an excess of the growth stimulating substance, a product of the cell's oxidation. This fluid is rich in growth stimulating substance. It stimulates not only the cancer cells to grow but also the normal cells. The cancer cells already adapted to it respond more quickly. In their growth, they then remove the nutrition and necessary substances from the other cells and destroy them. As to the cause of cancer, these observations suggest that cancer is not the result of any specific substances or group of substances. It is the result of some primary change either in the cell or the tissue which may be induced by any one of a number of widely different substances and conditions.

GRANULOMA VENEREUM (INGUINALE). M. GOLDZIEHER and S. M. PECK, Arch. Path. **1**:511 (April) 1926.

Seven cases of granuloma inguinale have been studied by Goldzieher and Peck. An organism that is biologically and morphologically identical has been observed in all cases. Pure cultures were obtained in five cases. The etiologic agent of venereal granuloma is termed *Bacillus venereogranulomatis* —a proper genus of the family *Bacteriacae*. The etiologic rôle of the organism described is supported by the results of complement fixation, allergic tests and animal experiments.

SYPHILITIC MYOCARDITIS IN THE RABBIT. W. H. BROWN and L. PEARCE, J. Exper. Med. **43**:501 (April) 1926.

In the course of routine postmortem examinations of rabbits infected with *Spirochaeta pallida*, six cases of pronounced granulomatous myocarditis were encountered by Brown and Pearce. Spirochetes were not demonstrated in the lesions, but the clinical history and the gross and microscopic appearance of the lesions seemed to warrant a diagnosis of syphilitic myocarditis. The lesions measured 1 cm. or more in diameter and histologically were practically identical with those described by Warthin in cases of syphilitic myocarditis in man. These are said to be the first cases of syphilitic myocarditis or of visceral syphilis in the rabbit that have been reported.

ENTOMOLOGIC EPISODE OF EAST AFRICAN CAMPAIGN. G. G. JOLLY, Indian M. Gaz. **61**:164 (April) 1926.

Being unable to control infection with jigger fleas in any other way, Jolly resorted to having the troops go barefoot, with daily foot inspection and the removal of jiggers. In a month's time the jigger scourge had practically ceased to give trouble. The success of this experiment depended on the fact that the jigger flea can only breed in the body of its host, and that daily inspection prevented this by detection and removal of the female jigger before it had time to develop its eggs. The victims of the parasites themselves became the trap that lured the jigger to its destruction.

THE CAMPAIGN AGAINST SYPHILIS IN BELGIUM. BAYET, Bull. de l'Acad. roy. de méd. **5**:608 (Nov. 28) 1925.

Bayet presents the results accomplished in Belgium since the Armistice as a brilliant success. At the close of the war the disease had spread to the remotest villages, and drugs to combat it were distributed through 300 clinics and dispensaries; but it was not until August, 1920, that a concerted effort was made for systematic drug prophylaxis on a large scale. As the arsenicals cause the rapid healing of the open lesions of syphilis, this double cicatrizing and microbicidal action reduces the contagious stage of syphilis to a fourth or a fifth of the former duration of the infectious phase. This is equivalent to reducing by 75 or 80 per cent of the number of sources of infection. The universal distribution of the disease compelled universal provisions for combating it, and the national public health service called on every physician in the realm for aid. The state supplied the drugs free to every person affected with syphilis, and medical treatment was given free also, the state reimbursing the physicians for their assistance in administering the drugs. In this way, treatment was accessible to all, and the entire medical profession throughout the country collaborated in the work. The state paid 1,400,000 francs annually for the drugs during the first years, and paid the expenses of the numerous preventoriums established.

In the Scandinavian countries, every syphilitic person is compelled to continue treatment until completely cured, under penalties up to imprisonment. But these measures are too drastic for Belgium, and the reliance had to be on measures to warn, persuade and remind syphilitic patients of the necessity for overcoming their inertia and continuing treatment as long as necessary. The Antivenereal Peril League conducted an intensive campaign with posters, meetings, pamphlets, moving pictures, reaching directly nearly a million and a half persons and rallying to the service 250 different organizations of various kinds; 100 lecturers delivered 2,250 lectures, during the three years, to audiences totalling 562,500. The work of the Antivenereal Peril League was thus an indispensible complement to the work of the state in the campaign, but the country physicians deserve special credit for searching out cases in the remotest regions. The proportion of new cases to the total number of syphilitic cases dropped from 25 per cent in 1920 to 12 per cent in 1923; in Brussels, from 23 to 9 per cent; at Antwerp, from 34 to 16, and at Liége from 34 to 12 in 1924. In no other country have the results been so decisive as in Belgium except in the Scandinavian countries. The propaganda made by the league was not on moral grounds but a propaganda of facts, bringing the secret diseases out into the open, proclaiming their dangers, and posting everywhere the addresses of places where they could be cured free of cost. Most of the new cases encountered now are imported.

FAMILIAL LOCALIZATIONS OF SYPHILIS. C. FLANDIN, Bull. Soc. méd. de hôp. **50**:243 (Feb. 19) 1926.

Flandin reports five cases of syphilis with identical localization in members of the family: syphilis of the aorta in two brothers and of the wife of one; in husband and wife, and in father and son; also hemolytic jaundice, from congenital syphilis, in father and two daughters. In his opinion, the syphilitic virus is single; its localization may depend on a hereditary predisposition, rendering certain tissues or organs more vulnerable, so that they became the elective seat of the spirochetes. The identical form of syphilis in husband and wife may possibly be explained by the same food and conditions of living, inducing in them similar properties, entailing analogous reactions to a morbid agent. The specific treatment cannot modify the tropism of the spirochete in the contaminated subject, but it may modify it in the one transmitting the infection.

PROTEIN TREATMENT IN SYPHILIS. A. CATALANO, Riforma med. **42**:369 (April 19) 1926.

Catalano injected intramuscularly at five day intervals from 5 to 10 cc. of boiled milk into persons with general paresis and tabes. Besides this he used bismuth. He failed in three cases of tabes, but had excellent results in five of eleven patients who had general paralysis.

ERYTHEMA NODOSUM AND TUBERCULOSIS. G. ARÁOZ ALFARO, Semana med. **1**:2 (Jan. 7) 1926.

Aráoz Alfaro asserts that erythema nodosum may be the manifestation of various infections, but tuberculosis can be incriminated in the majority. In certain cases it seems to be a primary affection representing an attenuated and masked form of tuberculosis. He has encountered another group of cases in which the erythema nodosum seemed to be the final episode in a fever continuing through several weeks in children with glandular disease and positive tuberculin test. In these cases, the erythema seemed to act like a fixation abscess, arresting the bacillary fever and materially improving the general health. One infant, 18 months old, had been having fever for two weeks and miliary tuberculosis was feared, but the discovery of a nodule on the leg suggested the possible onset of erythema nodosum, and he notified the parents that there would probably be a crop of them, with high fever, after which the child would be healthier than before. The course of the case realized his prophecy completely. In a second case of the kind the child was 2 years old, and both have been in much better health since the erythema a year and a half or two years ago.

MALARIA TREATMENT OF GENERAL PARALYSIS. G. BOSCH and A. MÓ, Semana med. **1**:25 (Jan. 7) 1926.

Bosch and Mó report results surpassing anything previously realized. Of their forty patients thus treated, 17.64 per cent have been attending to business for as long as two years up to date; 29.41 per cent have returned to ordinary home life, and only 20.58 failed to show benefit. One in advanced cachexia died, and another died after an operation for appendicitis. The others are still under treatment.

TREATMENT OF ANTHRAX IN MAN. F. DESTÉFANO and R. F. VACCAREZZA, Semana méd. **1**:165 (Jan. 28) 1926.

Destéfano and Vaccarezza analyze 414 cases of anthrax, tabulating the outcome. The mortality was 10.93 per cent in 192 cases in which a 5 per cent solution of peptone was injected intramuscularly once or twice a day until the general symptoms subsided. It was 15.85 per cent in the eighty-two treated exclusively with antianthrax serum, and 29.41 per cent in the seventeen treated exclusively with normal beef serum. Omitting the cases in which death occurred within two days, these figures become, respectively, 9.04 per cent for the peptone; 10.38 for the antiserum, and 25 per cent for the normal beef serum. The peptone parenteral protein therapy seems to be not only more effectual, but it does not induce serum sickness.

BLOOD SUGAR IN DERMATOSES. F. SIMON, Arch. f. Verdauung-Krankheiten **37**:363, 1926.

Simon found in psoriasis and furunculosis a higher level of blood sugar. Hyperglycemia is common in eczema, especially in chronic cases. Insulin treatment acts favorably sometimes, especially on the itching.

GANGRENE OF THE SCALP FROM BLEACHING THE HAIR. K. VON BERDE, Dermat. Wchnschr. **82**:257 (Feb. 20) 1926.

Von Berde gives an illustration of gangrene of the entire back of the head in a woman, aged 26, who had had her red hair bondined by a professional hairdresser ten days before. The woman had long been subject to eczema. The label on the empty bottle specified 30 per cent hydrogen dioxide. The woman wore a felt hat home, thus steaming the region further with the fumes of the chemical while the braids of hair were pressed by the hat on the irritated scalp. The pain was so severe as the woman walked home that she fainted. The region healed over in the course of three months, leaving a cicatricial bald area, 9 by 10 cm. in size.

LATENT SYPHILIS. W. KOLLE and E. EVERS, Deutsch. med. Wchnschr. **52**:557 (April 2) 1926.

Kolle and Evers inoculated rabbits with syphilis about four weeks after an injection of a bismuth suspension. The animals developed no symptoms. If the bismuth deposit was removed two or three months later, typical chancres developed. Other animals could be infected by inoculation of an emulsion from the popliteal lymph nodes of rabbits in which the syphilis was kept latent by bismuth. Experimental transmission of syphilis succeeds apparently in only 90 per cent of the animals, and only in a small percentage in direct transmission from man. Yet the popliteal lymph nodes of such apparently resistant rabbits are infectious. In one case, the chancre became manifest after inoculation with lymph nodes from an apparently immune rabbit that had been inoculated with the nodes from another rabbit which did not react. All this shows a close parallelism between the infection of rabbits and of man.

ACTION OF RAYS ON CELLS. R. GASSUL, Klin. Wchnschr. **5**:560 (March 26) 1926.

Gassul reports his observations with roentgen irradiation of tissue cultures. Daylight is one of the possible sources of error in such experiments. Explants of spleen tissue from normal frogs did not grow so well in the plasma from

irradiated frogs as similar tissue taken from irradiated frogs and cultivated in normal plasma.

SYPHILITIC AORTITIS. C. BRUHNS, Med. Klin. **22**:279 (Feb. 19) 1926.

Bruhns examined 200 syphilitic patients who had been infected from four to forty years before. He found that from 23 to 38 per cent of them had an unsuspected syphilitic aortitis. Early and energetic treatment is indicated.

PSYCHOLOGY OF ANGIONEUROTIC EDEMA. I. H. SCHULTZ, Med. Klin. **22**:573 (April 9) 1926.

Schultz' patient was a man dissatisfied with his wife but faithful to her. He had the habit of taking off each night the wedding ring he wore. On the morning after the departure of his wife for a three weeks' absence, he developed an angioneurotic edema of the ring figer, which made it impossible to replace the ring. The edema disappeared when the wife returned.

ROENTGEN-RAY TREATMENT IN SKIN DISEASES. L. FREUND, Wien. klin. Wchnschr. **39**:349 (March 25) 1926.

Freund emphasizes that it is as necessary to protect the deep tissues as the surroundings. It is not only superfluous, but injurious, to use hard rays on superficial skin diseases, such as psoriasis, eczema, or for depilation. He uses filters (0.5 to 3 mm. aluminum) only for depilation and for processes localized under the skin. The rays should be about 7-8 We. hard. He uses 6-7 We., without any filter, in psoriasis. Combination with other procedures — for instance, excision in lupus with irradiation of the open surface — improved the results. He is gratified with the success of roentgen treatment in favus and similar formerly extremely chronic affections. He does not mind that the articles still being published on it never mention the originator of the idea.

THERAPEUTIC MALARIA. J. DONATH and R. HEILIG, Wien. klin. Wchnschr. **39**:353 (March 25) 1926.

Donath and Heilig found remarkable differences between the changes induced by malaria and by other fever-producing agents. The amino-acids increase in the blood after injection of vaccines and proteins, but not in malaria. Contrary to this, the amino-acid content of the cerebrospinal fluid increases notably in malaria, less in relapsing fever and after typhoid vaccine, and not at all after injection of milk. They believe that a focal reaction of the central nervous system accounts for the favorable influence of malaria on general paresis.

POLYARTHRITIS IN A SYPHILITIC CHILD. P. NOBÉCOURT, Rev. méd. de la Suisse Rom. **46**:144 (March 10) 1926.

In Nobécourt's patient, a girl aged 15, the joint affection had started four years before, involving gradually the joints of the knees, ankles, wrists and hands. The lesions were bilateral and symmetrical, accompanied by atrophy of adjacent muscles and swelling of corresponding glands. The Wassermann test was positive in the blood. Under arsenical treatment the girl recovered; the joints became normal, the Wassermann test weaker. It is possible that joint lesions with congenital syphilis may be due not only to a local action

of the spirochetes, but also to a general dystrophy. Nothing to indicate derangement of function in any endocrine glands could be incriminated in this case.

EARLY HISTORY OF SYPHILIS. O. ECKSTEIN, Schweizer. med. Wchnschr. **56**:279 (March 27) 1926.

Eckstein reviews the early history of syphilis in China. He quotes a few passages published in 1632 by Chan-sze-ching. They are quite modern in the keen clinical observation and knowledge of extragenital and congenital syphilis. Mercury was used in treatment.

# Society Transactions

## BROOKLYN DERMATOLOGICAL SOCIETY

*Feb. 15, 1926*

B. THRONE, M.D., *Chairman*

SCLERODERMA AND SCLERODACTYLIA. Presented by DR. BERKOWITZ.

F. F., a woman, aged 39, had a fixed, drawn expression of the face; the cheeks were yellowish, rather taut and immobile; around the lips were many vertical lines giving the mouth a drawn appearance. The scalp showed marked alopecia with very fine dry hair. The arms were slightly red and rather hot to the touch, while the dorsa of the hands and fingers were cold, clammy and slightly cyanotic. The terminal phalanges and nails were nearly obliterated, leaving only about one-eighth inch of discolored brownish curved nail. The right fifth finger was contracted and very much more erythematous than the others. The skin was quite shiny. The fingers were all in a semiflexed position, with but about one third the normal motion present. The legs showed a bluish-red, cold, shiny surface, and the soles were cold and cyanotic. The right inner malleolus showed a large circular lesion about 2½ inches (3.7 cm.) in diameter, with slight scaling, exudation of serum and ulceration in the center. This lesion was apparently traumatic. The second and third toes of the left foot had been amputated, and the toe-nails of the other toes were practically obliterated. The great toe-nails were apparently normal. The patient, who has three healthy children, has been working as a rope spinner all her life.

### DISCUSSION

DR. ABRAMOWITZ: I have a patient with scleroderma of the fingers, and the only treatment that seems to help is baking followed by massage with cold cream.

DR. BERKOWITZ: At the Jewish Hospital there was a woman who had a generalized scleroderma; she was treated with sodium thiosulphate. There was marked improvement. She had been handling tapestries and wall paper many years before the scleroderma developed.

DR. ABRAMOWITZ: I saw the patient to whom Dr. Berkowitz referred. The tapestries which she handled contained dyes containing arsenic. A large percentage of arsenic was found in her urine, and for that reason she was given sodium thiosulphate.

DR. THRONE: I have two patients with scleroderma in whom arsenic was found in the urine. They both received sodium thiosulphate, and the improvement was satisfactory.

DR. WALZER: Owing to the fact that arsenic is one of the oldest drugs used, it seems to me there should have been a great deal more scleroderma resulting from it, if it is a cause of scleroderma. I think the use of arsenic or contact with arsenic and the appearance of the scleroderma is a coincidence.

DR. ABRAMOWITZ: Ayres first reported patients with scleroderma in whom arsenic was demonstrated. It is known that some forms of arsenic are more toxic than others; and then there is the question of idiosyncrasy. It may

require a long continued exposure to arsenic, a certain combination of arsenic and a peculiar idiosyncrasy to produce scleroderma. It is a subject which requires further study, and no definite conclusions can as yet be drawn.

PITYRIASIS RUBRA PILARIS? Presented by DR. CHARGIN.

B. H., aged 18, unmarried, a waiter, said that the eruption which he had had existed for ten years. He had been treated in various ways, but the eruption had never disappeared. With the exception of a few areas, the entire body was involved. The clear areas were on the extensors of the arms and legs, neck and numerous smaller areas over the back and abdomen. The scalp was scaly, but the hair seemed normal. The face was uniformly red and scaly. The scales were small, white, quite adherent and dry. The throat was especially involved, and showed many isolated and confluent keratotic papules. On the chest the eruption was red, and in broad bands, extending from above downward. The eruption was uniformly scaly, and for the most part no individual papules could be made out. On the abdomen and the back, the eruption was uniformly red, scaly and not infiltrated. On the extensors of the arms the eruption was similar to that on the back. The flexors were comparatively free, but showed numerous isolated small and larger patches. On the upper legs and on the buttocks, the eruption showed, in addition to the uniform redness, areas of keratotic papules. The lower legs showed isolated erythematous patches. The flexures of the elbows and knees were not involved. The backs of the fingers and toes did not show the characteristic keratotic papules. The palms and soles were normal. The nails were not involved. The mucous membranes were negative. Except for occasional slight itching, there were no subjective symptoms.

DISCUSSION

DR. ABRAMOWITZ: I think it is difficult to give a conclusive diagnosis in such a case. The patient has erythema and slight scalding on the face and scalp, and he presents on the body an eruption made up of many papules, most of which are shiny and scaly and very few of which are plugged. These are arranged like long strands. He has evidently had the condition for a long time. The flexors are free. There is no involvement of the nails and phalanges. In pityriasis rubra pilaris of so long duration, there should be some signs on the backs of the phalanges. It seems advisable to consider some form of ichthyosis or parapsoriasis.

DR. THRONE: I am inclined to agree with the diagnosis as presented. Darier's disease might be considered.

DR. CHARGIN: I do not make a definite diagnosis of pityriasis rubra pilaris, but when I consider all the clinical features in the case I am inclined to favor this diagnosis. Darier's disease did not occur to me. The papules in Darier's disease are more grouped and more conspicuous, and the distribution is different. The features in this case that suggest pityriasis rubra pilaris are the erythroderma of the face and body and the papules on neck, buttocks and upper legs. Against this diagnosis is the fact that the backs of the fingers and toes do not show the characteristic papules, but these may at times be absent in otherwise typical cases. Ichthyosiform erythroderma also came to mind, but the flexures of the elbows and knees are quite free from the eruption. Ichthyosiform erythroderma begins much earlier in life and, moreover, this patient presents typical keratotic papules.

(For additional discussion, see Transactions Section on Dermatology and Syphilis, New York Academy of Medicine for March 2, 1926.)

CHRONIC RADIODERMATITIS. Presented by DR. WALZER.

D. P., a married man, aged 31, who is an operator on cloaks, said that about ten years previously he had had "warts" on both palms and on the back of his right index finger which were present for one year before they were treated. In 1917, he received about ten treatments with the roentgen ray, during a period of four months. All "warts" on the palms disappeared, but within two years the skin of his hands became dry, atrophic, fissured and telangiectatic. Keratotic lesions were also present.

EXFOLIATIVE DERMATITIS OF THE EXTREMITIES. Presented by DR. HOWES.

The arms of C. K., a man, aged 35, a bookbinder, were both swollen and erythematous, with coarse scales on the forearms and large scaling plaques on the palms and fingers. The right foot appeared like the hands, and there was a hemorrhagic area on its plantar surface. He gave a history of having had eight attacks of this nature during the preceding nine months, the last of which involved the feet and legs. There was no arsenic in the blood or in the urine. The urine was negative. The Wassermann reaction was negative. Protein sensitization tests were negative. His blood pressure was 160 systolic and 80 diastolic. Roentgen-ray treatments had relieved the pruritus.

DISCUSSION

DR. BEERS: I saw a young woman some years ago who was very sensitive to fish glue. If she licked a label or handled glue and any of it got into her mouth, her mucous membranes would become inflamed and her tongue would become thickened to an extraordinary degree. Once she presented a generalized erythema.

DR. ABRAMOWITZ: I think this patient presents an ordinary dermatitis venenata. The eruption is definitely limited to the arm up to where the sleeves are rolled. I think the food protein tests in this case would prove useless.

DR. BEERS: Two years ago I saw eight men who were suffering from acute dermatitis on the forearms. They claimed that it was due to the use of phosphoric acid which they used in their work, etching on sheet tin. I went to the factory to see them work, and I found that the acid did not come in contact with their arms while working, but after work they all washed with a new kind of washing powder, and this we finally determined as the cause of the dermatitis.

KERATODERMA. Presented by DR. A. WALZER.

A. Z., a boy, aged 9, who had never been sick, gave no history of any skin disease in the family. His grandmothers were first cousins. The boy's father claimed that the following condition was of only about three months' duration. Each palm showed a large, sharply marginated erythematous, slightly verrucous patch which extended onto the dorsal surfaces of the fingers. The extensor surface of each elbow presented a silver dollar sized erythematous, slightly scaly patch, somewhat lichenified. The entire plantar surface of each foot was yellowish red; the skin was dry and thickened. This eruption involved both sides of the feet nearly to the malleoli. On each knee were patches similar to those on the elbows, triangular, with the base directed upward. Extending downward from the apex, to about the middle of the skin, were numerous, scattered, follicular, keratotic papules, some of which were surmounted by scales, the others having plugs or spines.

TUBERCULOSIS VERRUCOSA CUTIS. Presented by DR. HOWES.

J. R., a man, aged 37, married, a laborer in the building trade, noticed a small lesion on the dorsum of his right hand in 1918, which had increased in size. It had been treated with copper sulphate and silver nitrate. When presented, there were two quarter sized, verrucous lesions on the dorsum of the right hand which extended over the proximal phalanges of the index and middle fingers. There was occasional fissuring and exudation.

SYCOSIS VULGARIS CURED WITH INTRADERMAL VACCINE INJECTIONS. Presented DR. THRONE.

A man, aged 32, had suffered with sycosis vulgaris affecting both cheeks and extending onto the neck. In the *Bulletin de la Societe française de Dermatologie et de syphiligraphie* for May, 1925, p. 195, are the reports of two cases of sycosis vulgaris treated by intradermal vaccine injections and epilation. The cases were presented by Gougerot for Jean Meyer. Dr. Throne decided to determine the value of the vaccine injections alone, so that epilation was not done. At first an autogenous vaccine was used. This was not efficacious. Then a stock vaccine consisting of two billion each of *Staphylococcus albus, Streptococcus haemolyticus* and colon bacillus per cubic centimeter was tried. This was found to be entirely satisfactory. The injections were given intradermally, in the line of lymphatic drainage, in two places on each side of the face, or four injections at each treatment. The treatments were given every third day for six treatments, then at gradually increasing intervals. The patient shown had been under treatment for about six or seven weeks. He was cured. Most patients were cured. A few cases showed improvement only. A series of patients were treated with intradermal injections of a nonspecific protein to determine comparative therapeutic value. The injections were given intradermally on the flexor surfaces of the forearms. The results obtained with this were comparable with those obtained with the vaccine. The work was done at the New York Skin and Cancer Hospital.

DISCUSSION

DR. CHARGIN: My experience with nonspecific protein in the treatment of sycosis vulgaris has been disappointing.

ACNE VARIOLIFORMIS. Presented by DR. HOWES.

J. H., a man, aged 45, first discovered comedones throughout his scalp one and one half years ago. A few months later small abscesses developed. When presented, the vertex, occipital, and temporal regions showed numerous comedones, papules and pustules. In places the pustules had joined to form subcutaneous abscesses, with destruction of the hair follicles.

DISCUSSION

DR. ABRAMOWITZ: This case presents features that are usually absent in acne varioliformis. Acne varioliformis produces a small pustulonodular lesion that becomes dry and crusted, and when the crust falls off, a pitted scar remains. This patient shows some boggy lesions on the scalp which exude a fair amount of pus; this, and the grouping of the lesions, together with the undermining and the bogginess, resembles the disease described by Dr. Wise under the name of perifolliculitis capitis abdescens et suffodiens. The disease is rare, but I think this patient presents the condition.

DR. WALZER: I think this is a case of acne varioliformis. The lesions on the forehead and temporal regions are of the tuberculid type. The boggy masses present on the scalp I believe are scars with underlying pus.

DR. THRONE: I cannot find any lesions typical of acne varioliformis around the hair margins and am inclined to agree with Dr. Abramowitz' diagnosis.

A CASE FOR DIAGNOSIS. TINEA CIRCINATA? Presented by DR. HOWES.

S. T., a Jew, had had an eruption for nine months. The eruption began on the center of the forearm and spread slowly. It consisted of groups of papules and vesicles with erythema. The entire flexor surface of the right forearm and wrist was involved, and there were a few scattered vesicles on the left forearm.

DISCUSSION

DR. FRANK: I think that it is a case of dermatophytosis.

DR. ABRAMOWITZ: I think it is not a dermatophytosis, which diagnosis is being made too often. It is papulovesicular eczema. I suggest the use of Lassar's paste.

SCLERODERMA. Presented by DR. WALZER.

B. P., a woman, aged 38, married, had had two abortions and she has two living children. She had never been sick. Her present trouble was of ten months' duration. The eruption affected the lower extremities only, extending from the foot to the pubic region on the left side and to the middle of the thigh on the right side. Both thighs showed an erythema that varied from a faint pink to a dark violaceous color. The left knee, inner surface, showed a palm-sized, white, indurated patch. The skin over both ankles was tense, adherent and erythematous. The left thigh, posteriorly, depicted a palm-sized, dense, white patch. The skin was wrinkled and was covered with a fine furfuraceous scale. This patch was within the erythematous area.

DISCUSSION

It was generally agreed that this was a case of scleroderma, although later it might prove to be one of acrodermatitis chronica atrophicans.

PARAPSORIASIS. Presented by DR. CANTOR.

A girl, aged 14, complained of no subjective symptoms. Her mother had noticed the eruption four years previously, shortly after a Schick test was made on the child. Five other children in the family were subjected to the Schick test, however, and no eruption developed. The eruption, which was fairly generalized, consisted of discrete papules covered with fine scales. In places the papules suggested those of lichen planus.

DISCUSSION

DR. ABRAMOWITZ: I agree with the diagnosis. As to therapy, Dr. Wise reported one case of parapsoriasis in which the patient was treated with the Alpine light sucessfully. Pilocarpine has also been used in these cases. Recently, calcium chloride has been suggested for treatment.

E. A. GAUVAIN, M.D., Secretary.

## CHICAGO DERMATOLOGICAL SOCIETY

*Regular Meeting, Feb. 17, 1926*

E. P. ZEISLER, M.D., *President*

LICHEN SIMPLEX. Presented by DR. STILLIANS.

A white man, aged 53, gave a history of being bitten by a woodtick on July 1, 1925, the center of the bitten area being torn out when the tick was removed. This was followed by intense itching. The scab was torn off the wound, and he then noticed an elevation. The itching had persisted since that time, being especially marked during dressing and undressing.

In the right posterior axillary line there was a nodule 1 cm. in diameter, bluish-red, with a thin, pink scar on its rounded top. Extending for about 2 cm. around this nodule was a patch of brown pigmentation in which areas of lichenification could be seen, and beyond this patch were a few small areas of lichenification. Dermographism was not marked. The infiltration had been somewhat reduced by the application of a soothing lotion during one week.

DISCUSSION

DR. STILLIANS: I thought this case was interesting because of the history of the patient's having been bitten by a woodtick, with the subsequent formation of the patch of lichen simplex. The pathogenesis of the central tumor is not clear to me.

DR. DRIVER: I do not know that I can discuss the case, but I talked it over with Dr. McEwen and thought his idea was very good. There seems to be a question as to whether a woodtick leaves a foreign body. The man has some lichen simplex around the area, but the tumor seems to be large for a nodule forming on a lichen simplex. A foreign body tumor would, I believe, give such a picture as we see here.

DR. MCEWEN: It occurred to me that there might be a foreign body present in this case.

DR. FINNERUD: We had a similar case not long ago, and we froze the head of the parasite as well as the body. We thought the entire head was removed, but the patient returned a few weeks later with a firm pea-sized nodule, which disappeared with roentgenotherapy.

DR. STILLIANS: I asked the man whether the whole tick was removed, and he was sure it had been. I had thought of a keloid development also, for the development of the tumor impressed me as being very rapid. I have wondered whether it is not a reaction to a toxin that causes these tumors.

DR. FOERSTER: We have recently seen a keloid develop within three weeks after the removal of a mole. All along the stitch holes of the incision were keloidal proliferations. Anyone who has removed woodticks knows it is something of a task to get the insect out whole. I think the keloidal development is not atypical.

LICHEN PLANUS (CIRCINATE TYPE). Presented by DR. STILLIANS.

A white man, aged 45, said that ten weeks previously a small white spot had appeared on the side of the penis and slowly enlarged. Treatment with iodine and several mercurial ointments had been of no avail.

On the left side of the shaft of the penis was an oval ring of papules 3 by 2 cm. in diameter; the border was sharply elevated, 0.2 to 0.3 cm. wide and about half as high. They were a light brownish-red, firm to the touch. From this ring several short, linear projections, similar in character to the border, extended toward the center of the patch which was of normal skin color. About the center of the mucous membrane of the right cheek was a white-topped papule 0.1 cm. in diameter. There was no subjective symptom.

NOTE.—The patient absolutely refused a biopsy and did not return.

DISCUSSION

DR. FINNERUD: I thought strongly of the possibility of granuloma annulare. I have never seen it in this region, but understand several such verified cases have been reported. Dr. Foerster noted an adherent scale over the lesion, so the proper diagnosis probably is lichen planus annulare.

DR. MCEWEN: The pigmentation about the mouth seemed so unusual that the question came to me whether the man might not have a trace of colored blood in him.

DR. FOERSTER: The central lesion shows some pigmentation, which favors lichen planus annularis. An isolated lesion of lichen annularis would be very unusual. The question of granuloma annulare which Dr. Finnerud brought up must be given consideration. The extent, the narrow border and the lack of translucence or waxiness are against granuloma annulare. I think we need a biopsy to settle the question.

DR. STILLIANS: I recognized that annular lichen planus is much more likely to occur on the glans than on the skin. I will try to get a biopsy and report the result later.

HYDROA ESTIVALE. Presented by DR. FINNERUD.

A boy, aged 5, had had an eruption of the nose, cheeks, forehead and ears for ten months. The individual lesions were always blisters which ruptured spontaneously, appearing and disappearing within a week, but one or more lesions were always present. Similar lesions had occasionally been present in the mouth. In the summer of 1925, the child had had a similar eruption on the legs and front of the chest most of the time. The parts affected were those not covered by clothing. The urine had not been examined for hematoporphyrin.

DISCUSSION

DR. SENEAR: When the members of this Society saw this boy before, we considered the diagnosis of hydroa estivale. So far as the evolution is concerned, the condition is more like a recurrent impetigo than hydroa estivale.

DR. FINNERUD: We will try to get the proper urinalysis before the next meeting and report further.

LUPUS VULGARIS. Presented by DR. WAUGH.

A man, aged 41, had a disorder of fourteen years' duration. Two areas were involved, on the right cheek and neck. The larger lesion was about 2 in. (5 cm.) wide. The central portion was composed of rather thick scar tissue, the outer portion of slightly scaling, characteristic papules and nodules. The smaller lesion was of more recent development, but similar in character.

DISCUSSION

DR. MITCHELL: I agree with the diagnosis.

DR. MCEWEN: I was inclined to regard the condition as a lupus vulgaris, although it developed rather late.

DR. FOERSTER: As to the question of late development, I have seen lupus vulgaris develop after the age of 60 in several instances.

DR. ZEISLER: We have had two patients of about 60 who had lupus vulgaris erythematodes.

TUBERCULOSIS AND TUBERCULIDS. Presented by DR. LIEBERTHAL.

A Mexican woman, aged 40, was first seen two weeks ago at the Michael Reese Clinic. She was married and had given birth to six children, of which two (twins) were stillborn. Her present affliction began about two months ago with swelling of the left foot and a rash over the left leg. Soon afterward the right foot and leg showed similar changes, also the arms and mouth. She felt generally ill and had considerable pain in the mouth. She presented the following cutaneous and mucous lesions: On the posterior side of each tibia there was a hazelnut-sized, round, bluish-red, firm node such as is seen in erythema induratum; over her legs and arms were numerous papulonecrotic lesions; on the lower lip below the gum was an irregular, slitlike ulcer with undermined margins; the tongue in its anterior third was bright red and swollen, and on the tip and sides were pea-sized, pearly white, ulcerative lesions. There was no glandular enlargement. A Wassermann test of the blood proved negative, and the result of pulmonary examination was not conclusive. She received a provocative injection of neo-arsphenamine. The seroreaction proved negative again, but after this injection she improved very much.

DISCUSSION

DR. ZEISLER: I think the lesions in the mouth are not tuberculous, but rather some form of yeast infection. The lesions on the legs I think are those of erythema induratum.

DR. FOERSTER: Dr. Lieberthal said that the lesions had been changed somewhat by medication. The lesions on the tongue I think support the diagnosis of tuberculosis. Those on the legs and thighs were clinically such as we are accustomed to see in erythema induratum, but it occurred to me, considering the nationality of the patient, and that erythema-induratum-like lesions appear in leprosy, that this diagnosis should be ruled out.

DR. KINGERY: I think the lesions on the leg with the scarring were indicative of the diagnosis suggested. The lesions on the tongue I thought were in part due to contact with the teeth. Evidently some disease has been present for a long time, for there was a lot of atrophy, and the grayish-blue tint was a little suggestive of lupus erythematosus.

DR. LIEBERTHAL: Although the Wassermann reaction proved negative twice, there may be a specific incident in this case. If I can continue to observe the patient, I shall make further reports in due time. Several years ago I presented a patient before this Society with lesions of the lower lip, who showed all the earmarks of tuberculosis. That patient also had pulmonary tuberculosis. All the examinations in regard to the lip, pathologic, bacteriologic and animal

inoculation, however, proved negative. The patient was then placed in a sanatorium. With the improvement of the pulmonary and general condition, the lesions of the lip healed.

A Case for Diagnosis. Presented by Dr. Senear and Dr. Wein.

A farmer, aged 44, had lived in Chicago for ten years, and previous to that time had lived in North Dakota. He presented a lesion on the dorsal surface of the middle phalanx of the right little finger, which was first noted in November, 1924, following a scratch obtained while cleaning a urinal drain. Subsequently multiple lesions appeared on the forearm, arm and in the axillary region. The entire process extended over a period of eight months, the last lesion appearing in July, 1925. The condition had been stationary since that time, except for a lesion which developed on the left thumb following an injury in April, 1925, which had been discharging since then.

DISCUSSION

Dr. Eisenstaedt: Everything clinically points to sporotrichosis. If cultures are negative, I believe the next diagnosis to consider is tuberculosis.

Dr. Harry R. Foerster: The deep lesions with the cicatricial tissue adherent to the underlying periosteum are suggestive of cutaneous tuberculosis. Also, the fact that the man had a lesion on the opposite side of the other extremity would give weight to the diagnosis of that disease. I think, with Dr. Eisenstaedt, however, that it is a case of sporotrichosis with tubercular lesions.

Dr. Driver: I should like to have Dr. Eisenstaedt tell us what method he uses for securing the sporothrix.

Dr. Eisenstaedt: I have simply cultured the sporothrix and kept the cultures in a dark room on Saboureau medium. I have not used any of the newer mediums, but some of them are reported to be even more conducive to growth than the old.

Dr. Harry R. Foerster: Have any roentgenograms been made of the forearms and chest?

Dr. Senear: We have considered sporotrichosis and an inoculation tuberculosis as the two possible diagnoses. Dr. Otto Foerster suggested that we should think of tuleremia, as that condition might give a similar picture. Dr. Eisenstaedt's suggestion of a leptothrix infection as a possible factor is of interest, as one of the surgeons as the University suggested the same possibility, his opinion being based on experience with several more or less similar cases.

Note.—Tubercle bacilli were later recovered from inoculated guinea-pigs after the latter had become activated following the administration of potassium iodide.

Pyoderma and Dermatitis Vegetans. Presented by Dr. Oliver and Dr. Finnerud.

An Indian, aged 25, presented an eruption which began as a pustule on the left ankle two months previously. The skin over the entire body was rather deeply pigmented, the result of dirt, and over the arms, legs, anterior portion of the chest, abdomen and lower back were numerous, pea-sized, superficial

ulcers. When he entered the hospital these were crusted over and filled with pus. In the right axilla was an elevated, vegetating area which itched intensely. The roentgenogram and sputum were positive for tuberculosis.

DISCUSSION

DR. STILLIANS: I thought it was a case of vagabondism, with ecthyma scars. The broad band of pigmentation down the front of the abdomen is striking. I never saw such a localization of pigmentation in vagabondism, but think this is the most probable diagnosis.

DR. FINNERUD: We were interested in the papillomatous growth in the axilla, which I presume is due to dirt. Apparently it is the pyodermite végétante of Hallopeau.

DR. FOERSTER: The scars ceased abruptly at the hands, just about the wrist, and I think this should be taken into account in the diagnosis. The covered parts of the body are in the worst condition, and the uncovered portions in the best.

DR. OLIVER: At the County Hospital we see these cases of vagabondism frequently. Men who bathe as infrequently as this man develop the pigmentation just from dirt. This man has not bathed for almost a year. When he came in his clothes had to be cut off him. We thought the case interesting because of the development of this patch of vegetating dermatitis in the axilla.

DR. EISENSTAEDT: The feature that struck me as most peculiar was the small scars and crusts. In my opinion, we usually see these in less uniform type. The fungoid growth in the right axilla, being a single lesion, is also unusual, for these growths generally are described as occurring in the groins and anal area.

CONDYLOMA ACUMINATUM. Presented by DR. FINNERUD.

A man, aged 23, gave a history of contracting gonorrhea one year previously. Two or three small "pimples" developed on the under surface of the foreskin a month or six weeks after that disease was contracted. These had enlarged and fused with new similar lesions in the immediate vicinity, forming a vegetating mass of pigeon egg size or larger. The patient was presented because of the marked degree of involvement.

A histologic specimen, prepared by Dr. Orland F. Montgomery, was presented, which showed marked acanthosis of benign character and a dense lymphocytic and plasma cell infiltrate throughout the corium.

DISCUSSION

DR. EISENSTAEDT: This is not an unusual case of condyloma. Condylomas are usually seen in association with venereal disease but not always. I think the best thing to do would be to soak the mass in a mercurial solution, mercuric chloride 1:10,000, for a week and then to perform a circumcision.

DR. STILLIANS: Why not use the roentgen ray?

DR. FINNERUD: I recently heard that Dr. MacKee said it was of no value in these cases.

DR. OLIVER: We have frequently used roentgenotherapy on these large cauliflower-like growths in girls. Our results have not always been encouraging. We are now having them removed surgically.

## NEW YORK ACADEMY OF MEDICINE, SECTION ON DERMATOLOGY AND SYPHILIS

*Regular Meeting, March 2, 1926*

FRED WISE, M.D., *Chairman*

DEMONSTRATION OF CULTURES AND PHOTOGRAPHS OF SOME DERMOPHYTES. BY DR. HOWARD FOX.

Cultures of thirty species of *Microsporon, Trichophyton, Achorion* and *Epidermophyton* in 250 cc. flasks on Sabouraud's isolation medium were shown. Glucose had been used in place of the now unobtainable maltose. Hanging drop cultures were also demonstrated under the microscope. Photographs were then shown of direct microscopic preparations, cultures on solid mediums, hanging drop preparations and a few clinical cases. About three fourths of the cultures on solid mediums (Sabouraud's isolation agar) had been made on petri or stender dishes. This obviated the somewhat troublesome procedure of breaking the flask to obtain a photograph. The technician had succeeded in cultivating these organisms on petri dishes with a small incidence of contamination. This was contrary to the experience of Sabouraud who considered petri dishes unsatisfactory. In Dr. Fox's earlier work, photographs had been made through the flask, but were not so satisfactory as those made by removing the upper part of the flask or the cover of the petri dish.

DISCUSSION

DR. WEIDMAN: The impressions that came to me most forcibly in connection with Dr. Fox's presentation are two: First, completeness; that he has shown all of the phases of ringworm work, beginning with the extemporaneous preparations and going on to the gross cultures and appearance in microscopic preparations, all of which have been presented with photographic excellence. The second impression is that this demonstration should have come to you from a very busy practitioner, from one who is not essentially a laboratory worker. Up to recent times he was not engaged in active teaching work, and that he has found time to engage in this work is a commentary on his desire for first-hand knowledge, for knowledge's sake and without any prospect of immediate utilization. It is most refreshing.

Perhaps the most practical consideration in connection with ringworm culture work will come after asking the question: What is the use of all of it? Is it anything more than a very pretty plaything? Of course it is fascinating, and I would recommend it as an avocation for those who enjoy nature study. But apart from this, in a few instances the routine taking of cultures has been produtive of concrete practical results. Thus, I recall, a high-school girl who apparently had an ordinary ringworm of the nails. We cultured in a routine manner and recovered *Achorion schönleinii.* When she returned she denied that she had any scalp trouble, was indignant when we demanded to see her scalp, and belligerent when told that she had a full blown case of favus.

When *Achorion quinckeanum* is isolated, it should focus attention on mice, as in a case in which the favus developed while the patient was in the hospital. When fungus diseases occur in epidemics, it is very useful to know whether there is a certain source of infection. Thus, in one epidemic of mouse favus the source was found in wheat imported from Australia.

But the most important phase, mycologically, is in its relation to etiology —not so far as the immediate results are concerned, but through accumulating a store of facts which eventually may be analyzed, and from which deductions can be made which will increase our knowledge of ringworm.

Dr. Howard Fox: I feel pleased at the interest shown in this demonstration. There can be no doubt that much of this work is of only academic interest. It is certainly fascinating, however, and, as Dr. Weidman has said, may lead to something of more practical value. All of the immense amount of cultural work of Sabouraud with fungi is of less practical value to humanity than his demonstrating that ringworm of the scalp could be cured with the roentgen ray at a single sitting.

Erythema Annulare. Presented by Dr. Chargin.

M. K., a musician, aged 65, married, about a year previous to presentation developed a small bullous lesion on the upper left aspect of the chest, which in the course of two or three weeks increased in size to half an inch in diameter. During the next two or three weeks, a group of similar lesions appeared around the primary lesion; two months later a generalized annular eruption appeared, the lesions varying in size from half an inch to 5 or 6 inches (1.2 to 12.7 or 15.2 cm.) in diameter. The centers were clear; the periphery was made up of a narrow band from ¼ to ½ inch (0.6 to 1.2 cm.) in diameter and which contained very small vesicles. In the course of the second month the annular lesions disappeared, leaving a single palm-sized patch of eruption at the site of the primary lesion. This patch clinically resembled a neurodermitis. On account of the marked itching of this patch, the patient received several roentgen-ray exposures. While still under observation, three months after the disappearance of the generalized eruption, a recurrence took place, the eruption resembling that of the first attack. As the lesions were observed from time to time, it was noted that they spread centrifugally; as they developed into wider and wider circles, some ran together forming gyrate figures. It was also noted that the raised border, as it increased centrifugally, became less marked and finally lost its varied character, and the rings became broken up. There was considerable itching, especially in the area in which the primary patch appeared. The patient denied taking drugs. The Wassermann test was negative, and the urine was negative. Aside from the eruption, the patient was in a fair state of health.

DISCUSSION

Dr. Andrews: I am inclined to agree with the diagnosis. The appearance at first suggests mycosis fungoides, but the history is against that. I imagine it is some form of toxic erythema.

Dr. Levin: This case was most interesting to me because I had the opportunity to observe the man in Mount Sinai Hospital. Various diagnoses were suggested, but finally all agreed that it was erythema annulare or figuratum.

Dr. Wise: My first impression was that it was mycosis fungoides. The diagnosis of erythema annulare is one that may be taken or rejected; it all depends on one's first impressions. The fact that the man has severe itching is one point against erythema annulare, which is usually a nonitching condition. On palpation, the lesions are found to be elevated and indurated; the history is to a certain extent against mycosis fungoides on account of the remissions, but the possibility of lesions of mycosis disappearing spontaneously must be taken into consideration. I hope that it will be possible to obtain a biopsy.

DR. WOLF: I treated this man with the roentgen ray for neurodermatitis. After receiving two half-skin filtered units, he developed this generalized annular eruption. The eruption might be a toxic manifestation, having something to do with the roentgen-ray treatment; but the man stated that he had had a similar attack two months previously, which cleared up spontaneously.

DR. CHARGIN: Perhaps if we trace the history in this case it will help us to arrive at a diagnosis. The primary lesion, which appeared about a year ago, was bullous in character and was followed several months later by an acute outbreak of annular lesions, varying in size. These enlarged centrifugally, and in the course of several months disappeared. The present attack is also acute and numerous bullous lesions are present. Various diagnoses were considered by us, mycosis fungoides among them, but we thought that this could be ruled out by the bullous lesions, by the rapid appearance of the eruption and the comparatively rapid involution of the process. We look on this process as toxic in nature.

A biopsy will be taken and reported on at a later meeting.

A CASE FOR DIAGNOSIS: GRANULOMA ANNULARE? Presented by DR. GOODMAN.

J. C., a boy, came to the hospital on Jan. 28, 1926, complaining of lesions on the body and extremities which had been present for two months. Examination showed annular lesions on the left fore arm, three on the abdomen, four on the upper right thigh, three on the leg, one on the right foot, one on the upper left thigh, six on the leg and one on the dorsum of the left foot. The individual lesions were the size of a five-cent piece, with a raised border half an inch wide, a depressed center and a reddish color. The raised border seemed continuous, but on pressure was seen to be made up of individual papules. The color disappeared on pressure.

DISCUSSION

DR. HOWARD FOX: It looks like a disappearing eruption of granuloma annulare.

DR. ABRAMOWITZ: It seems to be a case of granuloma annulare, but a rather unusual one on account of the number of lesions. I had a case with about the same number of lesions. Most of them disappeared after two treatments with the alpine lamp. One lesion on the dorsum of the foot persisted, and I finally had to apply carbon dioxide snow, after which it disappeared. The mother had tuberculosis and the child gave a positive tuberculin reaction, and the roentgenograms of the lungs showed some healed fibrous lesions. I think that most of these cases of granuloma annulare are now being considered tuberculids.

A CASE FOR DIAGNOSIS: LYMPHANGIOMA? Presented by DR. GOODMAN.

Ida C., aged 26, a houseworker, presented above the inner canthus of the left eye, a group of deep-seated, thick-walled vesicles, the skin in the immediate vicinity being slightly reddened. The individual vesicles were pea-sized and smaller, with dilated capillaries passing over them. The redness was due to treatment with the Kromayer lamp.

DR. POLLITZER: I should not venture to make a diagnosis in this case without a biopsy, the more so as the condition has been modified by the acute erythema from treatment. The lesion looks to me like a small group of cysts or vesicles, and I should be inclined strongly to consider the diagnosis of lymphangioma circumscriptum.

DR. WEIDMAN: A somewhat similar case was shown at the last meeting of the Atlantic Conference, in which there was a group of vesicles at the inner canthus of the eye; and I have had a case in which the group occurred at the external canthus. The latter turned out to be (histologically) a lymphangioma. A remote alternative is a collagenous degeneration, akin to but not quite, colloid degeneration, because it is not yellow. I favor the diagnosis of lymphangioma, with the alternative of a mucinoid degeneration of collagen.

DR. HOWARD FOX: I agree with what Dr. Pollitzer said.

DR. ELLER: I would suggest the possible diagnosis of epithelioma, as the lesion seems to have more infiltration than is usually seen in a hydrocystadenoma.

DR. ABRAMOWITZ: I incline to the diagnosis of hydrocystoma. It is in the usual location for that disease; the vesicles are translucent, and the skin over them is quite thick. These lesions usually appear in hot weather or after exposure to a hot stove, etc. Although this is an unusual time of the year for these lesions to appear, and although no history of exposure to heat is obtained, the appearance of the vesicles favors the diagnosis of hydrocystoma.

DR. GOODMAN: I will obtain a biopsy and report later.

PEMPHIGUS. Presented by DR. WOLF for DR. SAYER.

A woman, aged 29, born in Poland, who had been married for twelve years and had two healthy children, who had had no miscarriages and whose husband was living and well, about three months prior to presentation complained of a burning sensation in the eyes, for which she sought advice. The condition was unaccompanied by any local lesions. A few days later, blebs appeared on the chest and abdomen, and then became generally distributed. The lesions consisted of round vesicles, pinhead to pea-sized and even larger. No itching was noticed.

When presented, there were bullous lesions on the buccal mucosa, and there had been bullous lesions on the vulva. There were bullae on the right cheek and on the dorsum of the right hand. The rest of the body was covered with crusted and foliaceous lesions in various stages of evolution. Nikolsky's sign was easily elicited.

DISCUSSION

DR. HOWARD FOX, DR. WERTHEIMER, DR. ROSTENBERG and DR. ELLER agreed with the diagnosis.

DR. CHARGIN: I agree with the diagnosis. Some of the bullous lesions are on an erythematous base. I have seen patients with lesions of clinically bullous erythema in whom the condition ended in true pemphigus.

DR. LEVIN: The patient presented typical lesions of pemphigus. The primary lesion is a bulla appearing on apparently normal skin. The erythema which may be seen is a secondary reaction.

DR. MALONEY: We had the patient under our care at Bellevue. The clinical picture was that of a typical pemphigus; she was given the Davis treatment for three weeks with improvement.

MELANOMA. Presented by DR. GOODMAN.

Mrs. M. G., aged 29, said that she had had the moles below the umbilicus all her life; seven months prior to presentation they became inflamed and began to enlarge. The group consisted of a central button-sized lesion.

elevated about three-eights of an inch above the skin, with four satellite lesions about its periphery, about the size of millet seed. The patient complained of pain in the left groin, but there were no palpable nodes; she was very stout. The color was brownish black.

DISCUSSION

DR. POLLITZER: It is a grave condition, involving the most serious possibilities for the life of the patient. The only thing to be done is to remove the lesion at the earliest possible moment. The method of removal is most important; if by surgery, it should be cut out widely, care being exercised not to handle it nor squeeze it with the forceps. If it is removed by one of the caustic methods or by electrocoagulation, the chances for the patient may be equally good, but I prefer pure surgery. The main point is that it should be removed at the earliest possible moment and not be handled; a very small amount of massage of the lesion may suffice to scatter metastatic cells with an inevitably fatal result. The prognosis in this case is grave.

DR. CANNON: I agree with Dr. Pollitzer about the necessity for removal, but I am not in sympathy with surgical excision. I think a more thorough removal can be accomplished with endothermy. About four years ago I removed a melanotic growth (about 3½ inches [8.8 cm.] in diameter, with surrounding satellite lesions) from a man's forehead with this method. Six months later, I removed a similar pea-sized area on the back of the scalp; and some months later a third one from his shoulder. A bad prognosis was given, but the man is still living and is perfectly well. I have had two other similar cases of melanoma, although less extensive, which were removed in the same way about three years ago, and neither of them has shown any evidence of metastasis. Sections taken from the growths in each instance showed melanocarcinoma.

DR. HOWARD FOX: My choice of treatment would be vigorous desiccation followed by the intensive use of the roentgen ray. I am not much in favor of surgical excision; many of the bad cases we have seen have followed this procedure. It is apparently possible to obtain a clinical cure by the roentgen ray alone, as was shown by a patient of MacKee's who was observed for ten years subsequent to treatment.

DR. ELLER: As we all know, the prognosis in the treatment of the black mole is always uncertain. Three months ago I saw a patient who had a bluish-black mole which had up to that time grown to twice its original size in three weeks. There were no enlarged glands or evidences of metastasis at that time. The growth was on the right cheek and was about three-eighths of an inch (0.9 cm.) in diameter. The lesion was completely excised with the endotherm knife, and an area 1 inch (2.5 cm.) in diameter and three quarters of an inch (1.8 cm.) below the surface was removed. When this tissue was studied microscopically it was thought that the prognosis was very good, for a great deal of fat was taken out and the black pigmented growth itself seemed to be encapsulated in a sac, which sac was not disturbed in the removal. The fat, on gross study, showed no evidence of pigmentation, but under the microscope cells containing black pigment were demonstrated. The great difficulty in treating these cases is that we cannot ascertain in advance how much tissue to remove, for the pigment-bearing cells may be one-half inch or many inches from the growth which is apparent on the surface. I

examined the woman two weeks ago and at that time there was a black scab on the surface, which appeared to be the same as the original growth.

NOTE: Since the report at the meeting, I have again examined this patient. The black scab has disappeared and the wound seems free from any evidence of the disease. I will report the progress of this case again in a few months.

DR. MCCAFFERTY: A few weeks ago a surgeon referred to me a patient with a pigmented mole undergoing degeneration. He advised against excision, as he had excised a few of these moles with a fatal outcome in each case, and asked me to use electrocoagulation. I did so and the immediate result was excellent. According to Clarke, electrocoagulation is different from desiccation; for coagulation, we use the d'Arsonval current, which is lower in voltage and higher in amperage than the desiccation current. Coagulation is more penetrating and intense than desiccation; therefore the destructive action is much greater. This patient is under observation, and a report of the final outcome will be made at a later date.

DR. ANDREWS: I would not like to see this discussion closed without the mention of radium. Three years ago, Dr. MacKee treated a patient with radium only, and there has been no recurrence. Also, at the Memorial Hospital, where we treat many patients who have these lesions, the method of choice is radium. A large dose is given over a very wide area. The results are excellent. I think that in a case like this the method would be to give an intensive exposure with radium (15 millicurie hours, filtered through brass at 1 cm. distance), and later to excise it to a wide extent with either an endotherm cutting current or with surgery.

DR. ROSTENBERG: Should the ordinary black mole be destroyed or untreated?

DR. POLLITZER: Melanotic lesions located where they are subject to irritation should be removed before they show evidence of degeneration. Of course, after they show signs of degeneration they should be removed promptly. Otherwise, unless there is some special indication arising from location, etc., they should be let alone.

DR. WISE: One of the important points to be considered is whether the moles have any hair on them. Moles with hair seldom undergo malignant degeneration; whereas the blue-black, hairless moles that are smooth and glistening are more likely to do so. Every patient who has been under my observation has died from metastases following malignant activity of the primary melanoma.

DR. ABRAMOWITZ: Dr. W. W. Keen of Philadelphia states definitely that under no circumstances should the pigmented nonhairy mole be let alone; it should be removed with the entire thickness of the skin (J. A. M. A. **85**:1577 [Nov. 14] 1925).

PITYRIASIS RUBRA PILARIS. Presented by DR. CHARGIN.

This case (B. H.) is published in full in the ARCHIVES as part of the Transactions of the Brooklyn Dermatological Society for Feb. 15, 1926.

DISCUSSION

DR. POLLITZER: I do not agree with the diagnosis of pityriasis rubra pilaris, for there were no horny plugs in the hair follicles, and it is especially noteworthy that the terminal phalanges were free from this characteristic follicular keratosis. I thought of the possibility of an atypical ichthyosis; the arms and legs especially suggested that diagnosis; but the character of the lesions on

the trunk suggested the diagnosis of parakeratosis variegata. There are areas on the back especially which are fairly characteristic of that disease, areas where there is a network of infiltrated, raised, smooth, red, slightly shiny tissue with clear areas in the middle.

Dr. Howard Fox: I agree with Dr. Pollitzer that this is not a case of pityriasis rubra pilaris. There is not only an absence of accuminate horny papules, but the palms failed to show the keratotic thickening that is characteristic of this disease.

Dr. McCafferty: I do not believe that this is a case of pityriasis rubra pilaris. The patient does not show keratoderma of the palms nor follicular papules on the first and second phalanges, so characteristic of the disease in question. I recently saw a child, 3 years old, with a definite dermatitis of the face, eczematization of the forearms, keratoderma of the palms and a follicular keratosis of the body. This case proved to be one of pityriasis rubra pilaris.

Dr. Abramowitz: I saw the patient at the Brooklyn Dermatological meeting about two weeks ago, and there has been a marked improvement since then, which is unusual in pityriasis rubra pilaris. I agree with the remarks made by Dr. Pollitzer.

Dr. Levin: I think that pityriasis rubra pilaris is the most probable diagnosis. The patient showed a generalized inflammatory hyperkeratotic, follicular, papular eruption, patches of psoriasiform lesions, and presented the nutmeg-grater-like sensation when the skin was palpated. Were the so-called characteristic papules on the dorsum of the fingers found, none would hesitate to make the diagnosis as presented.

Dr. Wise: My ideas are very similar to those expressed by Dr. Pollitzer. The absence of tylosis and hyperkeratosis on the palms is against the diagnosis of Devergie's disease. Instead of being a simple ichthyosis, I think it is an ichthyosiform erythroderma. The illustrations in the article published by Dr. MacKee and Dr. Rosen show these peculiar longitudinal striae on the abdomen which are characteristic of erythroderma of the ichthyosiform type. The reddening of the cheeks is characteristic; the history is in favor of that diagnosis. Whether or not a biopsy would clear up the diagnosis to any extent, I doubt. A biopsy from the side of the neck might show follicular keratosis which would be very much like that seen in ordinary ichthyosis or in keratosis follicularis; however, if a biopsy were taken from the striated area on the chest, it is possible that the histologic picture would be similar to that described in MacKee's article. So the choice of the locality for sectioning would be of some value in determining the diagnosis.

Dr. Chargin: I am willing to agree that this patient does not show all the characteristics of pityriasis rubra pilaris, but I maintain that the objective symptoms and the history favor that diagnosis more than any other. In parakeratosis variegata one does not observe the picture that this patient presents on the scalp and face. The mottled appearance seen in parakeratosis variegata is absent in this case. Ichthyosiforme erytheroderma starts much earlier in life, usually during the first year. To me, the patient does not show any evidence of ichthyosis; on the contrary, the primary eruption on the neck and on the buttock and thighs, is composed of keratotic papules, and I think that the uniform eruption which this patient presents is a confluence of these keratotic papules. The characteristic keratosis of the palms and soles and the keratotic papules on the fingers and toes are absent, but aside from this the

general picture fits pityriasis rubra pilaris better than any other entity. The point raised by the chairman about the striate distribution on the chest is also observed in pityriasis rubra pilaris.

ANAL CHANCRE? Presented by DR. PAROUNAGIAN and DR. MASON.

J. W., a youth, aged 19, was seen at the clinic on Feb. 27, 1926. He presented a generalized, unusual type of eruption with impetiginous lesions on the face and neck. The lymphatic glands were swollen below Poupart's ligament, and an examination of the anal region revealed a typical chancre. A dark-field examination was positive.

DISCUSSION

DR. HOWARD FOX: I do not consider that Dr. Parounagian has proved that the anal lesion is a chancre. The patient has been under observation only a few days and presents an ulcerating anal lesion in conjunction with a maculo-papular eruption. He also presents numerous excoriated papules suggesting a complicating scabies, but that is not the point under discussion. I feel that there is not sufficient evidence to warrant calling the anal lesion a chancre. If the patient had been under observation from the outset and the anal ulcer had been followed in proper sequence by general adenopathy and the secondary eruption, the diagnosis would have been clear.

DR. PAROUNAGIAN: Anal chancres are quite common. I have seen as many as three in one afternoon. I admit that the patient had condylomas, but when the parts were thoroughly stretched we detected a sharply circumscribed, eroded lesion in the anterior commissure, which was a typical chancre. Ordinary condylomas are elevated lesions covered with mucopurulent secretions, not a single eroded ulcer as in this case.

MILIARY PAPULAR SYPHILODERM. Presented by DR. PAROUNAGIAN and DR. MASON.

A Porto Rican, aged 29, presented himself at the clinic on Feb. 27, 1926, with a generalized, grouped, follicular, papular eruption which was said to be of two weeks' duration. He had no evidence of a genital chancre. He said that about two months previously he had had an operation on this throat (possible tonsillar chancre).

ACQUIRED SYPHILIS IN A CONGENITAL SYPHILITIC? Presented by DR. PAROUNAGIAN and DR. MASON.

F. H., aged 24, was admitted to the Bellevue syphilis clinic on June 4, 1925, having been referred from the throat service of Bellevue Hospital. At that time he gave a history of having had a genital sore one year previously. He had an ulceration in the throat, and his Wassermann reaction, made on May 24, 1925, was ++++. Further examination revealed a high vault, imperfect hair line, protruding forehead, a marked "tubercle of Mibelli" on the left molar, and a pronounced hemiatrophy of the face. He received eight injections of silver arsphenamine and fifteen of mercuric salicylate from June 4 to Sept. 22, 1925. Six weeks after the discontinuance of treatment, his Wassermann reaction was still ++++. He then received six injections of neo-arsphenamine and fifteen more of mercury, the last one being on the evening of presentation. Attention was called to a perforation of the hard palate which was of uncertain duration.

DISCUSSION

DR. CHARGIN: The patient has acquired syphilis, but I cannot agree with the statement that he also presents evidence of congenital syphilis. Assuming that he has tubercles on the molars, that he has a high arched palate and an imperfect hairline, that does not warrant us in making a definite diagnosis of congenital syphilis. The stigmas on which we usually make this diagnosis are apparently absent in this patient. It may be that he is the son of parents who had syphilis and that he has inherited stigmas of degeneration, such as has been described especially by Fournier, but strictly speaking this is not congenital syphilis.

DR. PAROUNAGIAN: I have often presented similar cases and expressed my opinion and observations regarding them. At one of the Manhattan Dermatological Society's meetings when I presented ten patients with either both parents, or brothers or sisters, having positive evidence of syphilis with ++++ Wassermann reactions, interstitial keratitis, or gumma of the tongue, moist papules at the angle of the mouth, etc., the majority of the patients presented the following stigmas or abnormalities: high vault, imperfect hair line, protruding forehead, and the tubercle of Mibelli. Those who claim that we get these abnormalities in rickets, tuberculosis, malnutrition, etc., ought to present such cases to prove that I am mistaken.

LICHEN PLANUS ATROPHICUS. Presented by DR. ANDREWS.

A. F., aged 36, an Italian, came to the Vanderbilt Clinic on Feb. 20, 1926, with an eruption of six months' duration. On the right side of the neck was a pigmented area with atrophic red lesions, accompanied by itching. In the left femoral region was a pigmented area with marked violaceous efflorescent papules which also were pruritic. Scattered over the trunk and extremities were pea-sized atrophic pigmented lesions. On the left buccal mucosa was a white pinhead-sized lesion.

PERNICIOUS ANEMIA—GLOSSITIS. Presented by DR. LEVIN.

G. P., a West Indian, aged 47, was admitted to Mount Sinai Hospital three months previous to presentation complaining of great weakness and a loss of 40 pounds (18.1 Kg.) in weight. The patient had syphilis. On admission, the symptoms were mainly those of cancer of the stomach, but the gastric symptoms cleared up under antisyphilitic treatment. The blood findings were characteristic of pernicious anemia. The tongue depicted smooth atrophy.

DISCUSSION

DR. WISE: It is a question whether the smooth atrophy of the tongue is due to syphilis or to pernicious anemia.

DR. WEIDMAN: From simple observation of this tongue, I do not believe that one could determine whether the changes were due to syphilis or to pernicious anemia. However, the latter is very possible because we all know that a chronic atrophic gastritis is found at necropsy in such cases, and that there is a very close connection between morbid changes in the stomach and the tongue. Furthermore, a hyperchlorhydria is often present in such cases; determination of this point would help secure the diagnosis of the tongue condition.

ATROPHY OF THE TONGUE FROM PHENOBARBITAL. Presented by DR. LEVIN.

This patient was presented before the section on April 4, 1922, at which time she presented bullous lesions of the tongue due to phenobarbital. She now exhibits areas of atrophy and white patches that resemble leukoplakia.

DISCUSSION

DR. ANDREWS: The case suggests syphilis of the tongue, and the woman said she had had a blood test at Mount Sinai Hospital and had received six injections of a yellow liquid into the arm.

DR. CHARGIN: The patient presents an atrophy, which is the end stage of the repeated attacks of bullous lesions produced by phenobarbital. The patient is not a syphilitic, and her Wassermann reaction has never been positive. We have watched this process from the beginning to the present time.

ARSENICAL DERMATITIS FOLLOWING ARSPHENAMINE. Presented by DR. WOLF.

A woman, aged 23, developed an initial lesion in the latter part of December, 1925. She received two injections of arsphenamine from a private physician, and then appeared at the Mount Sinai Clinic presenting the remains of an initial lesion of the upper lip and a generalized papular syphilid. One week prior to presentation, having received the sixth injection of arsphenamine, she developed a papulovesicular eruption on the upper extremities and chest, and slightly on the face.

DISCUSSION

DR. POLLITZER: I call attention to the fact that the eruption appeared after the sixth injection of arsphenamine. It is only after a long series of injections that arsenical dermatitis occurs.

DR. OCHS: I call attention to the fact that the patient has a goiter. There are several cases on record of arsphenamine dermatitis occurring in cases of hyperthyroidism. It may be possible the latter causes goiter susceptibility to arsenic.

DR. LEVIN: I cannot see any relation between thyroid or pituitary dysfunction and the eruption from arsphenamine. It is possible that arsenic may stimulate gland activity as well as the epithelium of the skin, and increase the tendency to inflammation. Endocrinologists consider that syphilis affects particularly the pituitary type of person.

EPITHELOMA OF THE FLOOR OF THE MOUTH. Presented by DR. ELLER.

This patient had been presented before the section eight weeks previously. The patient was presented again to show the result to date of treatment by burying radium emanation seeds in the growth and cross-firing with filtered roentgen rays to the adjacent glands. The lesion had disappeared.

GRANULOMA INGUINALE. Presented by DR. PAROUNAGIAN and DR. MASON.

C. D., an American negro, was admitted to Bellevue clinic on June 4, 1924, giving a history of an initial sore some seven years previously, for which he had had local treatment only. He afterwards was circumcised. An ulcer about the size of a silver dollar appeared on the pubic region four years ago. His Wassermann test was + on admission; and two years later, examinations were negative. He said that prior to his visit to the Bellevue clinic he had had

fifteen injections of tartar emetic, which healed the ulceration, but it returned six months later. He also received fifteen injections of tartar emetic from Aug. 14, 1924, to March 1, 1926.

INITIAL LESION OF PUBIC REGION. Presented by DR. LEVIN.

P. P., a plumber, aged 27, unmarried, noticed a sore in the pubic region one month prior to presentation. The lesion consisted of a bean-sized, round, hard nodule, with a clean ulcerated center. He complained of sore throat and headache, and presented a generalized macular eruption.

ERYTHEMA AB IGNE. Presented by DR. ABRAMOWITZ.

M. D., a man, aged 45, came to the Vanderbilt clinic on February 5 with an eruption on the back of the right thigh of ten days' duration. It consisted of a red patch 10 by 6 inches (25.4 by 15.2 cm.). It was configurated and reticulated and slightly ulcerated in places. The patient had a habit of standing close to a gas stove.

OSCAR L. LEVIN, M.D., Secretary

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## PHILADELPHIA DERMATOLOGICAL SOCIETY

*Regular Meeting, March 5, 1926*

J. H. STOKES, M.D., *Presiding*

A CASE FOR DIAGNOSIS. Presented by DR. WHITE for DR. STOKES.

C. M., a man, aged 34, married, had had bilateral deep ulcerated lesions on the dorsa of the feet for a month. Biopsy showed chronic inflammation. Serology was negative. Fixed dressings were applied, but the ulcers did not yield.

DISCUSSION

DR. GREENBAUM: My impression is that this is a traumatic ulcer with secondary infection.

DR. STOKES: We could find no reason for the lesion. The interesting feature is the bilateral configuration.

DR. WRIGHT: Sometimes a simple traumatic lesion develops into a lesion of this character. I saw a case in which there was a deep lesion that started as a simple traumatic abrasion, the lesion developing into an ulcer in three or four days, apparently as a result of secondary infection.

DR. WHITE: This patient's wife told me that the patient came home intoxicated, and she thought that he had caught his feet in the bed springs during the night.

A CASE FOR DIAGNOSIS. Presented by DR. WRIGHT.

N. M., aged 48, a man, in May, 1925, noticed a small ulcer on the calf of the right leg. There was no history of trauma. This enlarged to the size of a quarter, and in about six weeks, it healed. In December, 1925, another one appeared on the lower part of the right thigh. This healed in six weeks. Five weeks ago another appeared in the middle of the right thigh, a circular, clean

ulcer with a clear granular base and elevated edge, with very little discharge. Surrounding this ulcerative lesion was a diffuse erythemovesicular zone extending from the groin to the knee, apparently the result of too strong local applications. There was a shotty bilateral inguinal adenitis.

DISCUSSION

DR. SCHILDKRAUT: I consider it a dermatitis with secondary ulceration from scratching.

DR. HIRSCHLER: It makes me think of granuloma pyogenica. The patient may have had a dermatitis prior to the ulceration.

DR. WRIGHT: The only thing I have seen like this is an ulcer on the leg produced by a drop of croton oil.

DR. STOKES: A patient of mine, whom I saw three or four weeks ago, had a lesion that was practically the twin of this one. The patient had been pricked by a cactus spine, and an ulcer followed. Subsequently I have seen three or four other ulcers in the lymphatic distribution. They disappeared with the application of tincture of green soap, ammoniated mercury and one fourth of a skin unit of roentgen ray. It was probably ecthyma. One should not take it for granted that such lesions are pyogenic, for sometimes sporotrichosis looks like this, and can be picked up only by culture.

HYDROA AESTIVALE. Presented by DR. WHITE for DR. STOKES.

R. S., a boy, aged 4½ years, had a recurrent vesicular eruption on the face and exposed parts of the body for almost three years. It recurs in the spring and continues through the summer. The mother described them as being vesicular, leaving small punctate smooth scars. The general health was good. Other examinations were negative.

DISCUSSION

DR. GREENBAUM: I agree with the diagnosis. Two or three years ago I did some experimental work on such a patient. The mother claimed that the child became worse when she was exposed to heat. That would suggest an infra-red reaction, yet when I tested the child to the ultraviolet and roentgen rays, there was marked reaction. That case did not show hematoporphyrinuria.

DR. STOKES: I should like to know what experience the members have had in regard to the finding of hematoporphyrin in the urine in hydroa aestivale.

DR. GREENBAUM: The urine was studied carefully in his case, and none was found.

DR. HIRSCHLER: The mention of infra-red rays recalls to me that infra-red rays completely stopped the pain of herpes in the mouth.

DR. STOKES: An ordinary bathroom heater with a red spool produces as good results as the expensive apparatus for producing infra-red rays.

SCHAMBERG'S DISEASE. Presented by DR. SCHILDKRAUT.

J. S., a man, aged 28, a year ago noticed the development of some fine dot-like lesions on the outer side of the ankles. They spread and fused. There was left a brownish pigmentation. At the borders of the lesions were many minute punctate dilated capillaries.

DISCUSSION

DR. WRIGHT: I believe that Dr. Schamberg would concur in the diagnosis, although many pigmentary lesions on the leg are erroneously diagnosed as progressive pigmentary dermatosis are the result only of stasis. In a case shown recently there was marked excess of cholesterin in the blood, the meaning of which was obscure. There is often a yellowish cast to the central part of the lesions.

DR. HIRSCHLER: The lesions may involute spontaneously, this having been the result of other cases.

CASE FOR DIAGNOSIS. Presented by DR. WHITE for DR. STOKES.

H. B., a girl, aged 16, had symmetrical verrucous linear lesions on the ends of the fingers and keratotic lesions on the feet for nine years. The Wassermann reaction was negative. She had had a tuberculous cervical adenitis, and the chest showed an old healed apical lesion on the right. Gynecologic examination was negative for gonorrhea.

DISCUSSION

DR. WEIDMAN: I saw this patient twice. In another case of a child with keratotic lesions on the feet, the diagnosis was thought to be either linear nevus or tuberculosis verrucosa cutis. Biopsy showed granulomas under the epiderm—not clear-cut tubercles—more like those found after the introduction of foreign bodies. In some of the giant cells there were large blue bodies four or five times the diameter of a polymorphonuclear leukocyte. I believe that there was some foreign structure in the corium, causing a foreign body reaction. Elastic tissue may undergo degeneration in the skin, acting as a foreign body. In pseudoxanthoma elasticum, the elastic tissue may swell up, and take the form of balls. The result of guinea-pig inoculation from this patient has not been reported, and such a report must be awaited, to exclude tuberculosis verrucosa cutis. There is a definite history of tuberculosis, and that should be given weight, but the absence of any notable hyperemia at the base of the lesions and the definite form and symmetry of the lesions would cause me to incline toward the diagnosis of linear nevus.

DR. GREENBAUM: I regard the case as one of keratoderma, very much limited.

DR. STOKES: I have reached the conclusion that this is a symmetrical keratoderma, nevoid in character.

XERODERMA PIGMENTOSUM. Presented by DR. SCHAMBERG.

C. S., a youth, aged 18, had been under observation for fifteen years. He had a brother suffering from the same condition. He presented the classic picture of a xeroderma pigmentosum, with no particularly active lesions. Literally hundreds of carcinomas had been removed by electrocautery, radium, etc. Some years ago he had had a remarkable growth from the top of the scalp, which on excision was found to be myxoma, thus proving that there may be a variety of growths. The case was interesting in that it had been held in check only by constant surveillance. He had corneal ulceration and scarring from ectropion, pigmentation of the conjunctiva and pigmentation on the backs of the hands and forearms. His mother and father are first cousins. Both a Japanese and a Viennese physician have alleged that consanguinity plays an important part in this condition. In the literature there is an astonishing

number of instances in which there was close relation between the parents. In these patients the sun rays produce the effect of roentgen rays on normal skin. In this patient, the skin on the covered parts of the body is relatively normal, although rather dry.

DISCUSSION

DR. STOKES: I should like a discussion as to preventive measures.

DR. WEIDMAN: Dr. Schamberg has shown two patients, and I have shown one before this society on the same night. In these patients the type of carcinoma was different; Dr. Schamberg's patient showed the prickle cell type, and mine a basal cell. I should like to know about the blood typing of the parents and the patient, and about evidences of excessive destruction of blood.

DR. SCHAMBERG: I counseled the patient to use a heavy calamine lotion when he goes outdoors as a protection against the sun. I was present when he was presented before the American Dermatological Association, at which time Dr. Pusey humorously suggested Pittsburgh as a good place for such patients to live. I knew nothing about attempts to study the blood types of the parents, but some attempts had been made to determine any increase in porphyrin in the urine. No pathologic amount was found. These cases are tragic; in one family, seven children suffered from xeroderma pigmentosum.

DR. GREENBAUM: What is the relationship between the case of xeroderma pigmentosum, the case of hydroa aestivale and the allergies described by Duke?

DR. WEIDMAN: I do not recall that Duke covered the matter of the appearance of porphyrin in the light sensitive cases, but it is well demonstrated that rats may be sensitized to light by injection with porphyrin.

DR. SCHAMBERG: We must recognize several conditions in which there is hypersensitivity to the actinic rays of the light. In hydroa there is an inflammatory condition, and in the conditions described by Duke there was an allergic reaction. In xeroderma pigmentosum there is a degenerative and neoplastic reaction. Although these are all cases of hypersensitivity to light rays, yet the reaction is different.

A CASE FOR DIAGNOSIS. Presented by DR. MARKOWITZ.

C. J., a man, aged 50, had lesions on the dorsum of the foot for two and one-half years, with raised body and central involution. There was no itching. There were smaller lesions also. The lesions began as small nodules, and spread.

DISCUSSION

DR. GREENBAUM: I would diagnose granuloma annulare.

DR. SCHAMBERG: The case is unusual on account of the considerable diameter of the patches—larger than a half dollar. This case reminds me of the case of a young woman with raised plaques on the backs of the hands, without any central involution, with no diagnosis made. The two cases are almost similar.

DR. WEIDMAN: These lesions are more edematous than in other cases. How widely do the lesions of granuloma annulare vary in size? Dr. Corson showed a case with a very large ring, a section of which showed the histology of granuloma annulare.

DR. SCHAMBERG: I would suggest the roentgen rays as a therapeutic measure.

DR. STOKES: The lesions sometimes disappear without treatment; 25 per cent resorcin will aid in some cases. Roentgen-ray treatment is effective.

VON RECKLINGHAUSEN'S DISEASE, WITH PITUITARY DYSFUNCTION. Presented by DR. WHITE for DR. STOKES.

H. H., a youth, aged 18, for seven months had dim vision, headaches and slight acromegalic features. He had multiple subcutaneous nodules and a loose condition of the skin in the pretibial regions.

DISCUSSION

DR. SCHAMBERG: I agree with the diagnosis. The condition on the leg might be described as dermatolysis. The skin hangs in folds, and may be stretched considerably. It might be a nutritive disturbance. The fact that it is associated with dyspituitarism is interesting, for many have thought that multiple fibromas are associated with dysfunction of the ductless glands. One such case—more acute—was described by Dr. B. C. Hirst as occurring during pregnancy, and disappearing after pregnancy had terminated.

DR. GREENBAUM: The pituitary disturbances might possibly be the result of lesions in the pituitary gland similar to those in the skin.

DR. WEIDMAN: I would call attention to the comedones. I recall the case of a boy with many comedones, in whom there was enlargement of the sella turcica. That patient was also mentally inferior. I believe there is some relationship between the ductless and sebaceous glands.

LUPUS ERYTHEMATOSUS. Presented by DR. SCHAMBERG.

A young woman with lupus erythematosus, previously presented before the society, had recently had an acute diffuse dissemination. When she had presented herself she had a rather bluish-red superficial discoloration of the face—lupus erythematosus. Later an extension to the breasts occurred. She suddenly developed a temperature of 104 F., followed by distinct pemphigus-like bleb formation. The blebs ruptured, leaving superficial ulcerations. Respirations were accelerated to 50 per minute. Internists examined her chest, with negative findings. Nothing wrong with the viscera could be found. Roentgen-ray examinations were negative. The urine contained albumin and casts. She died, and necropsy was refused. The point of interest was the question of tuberculosis. She had a leukopenia, 3,500 white blood cells, and despite protein therapy the count did not rise.

DISCUSSION

DR. STOKES: A patient of mine with lupus erythematosus had a most amazing leukopenia over a period of weeks. This patient had only 1,900 white blood cells.

DR. SCHAMBERG: What about the appearance of blebs?

DR. STOKES: I saw one case in which a bullous erythema multiforme occurred as a part of the picture of erythematous lupus. But that was perhaps another condition altogether. In two cases at Johns Hopkins Hospital recently, I was told that guinea-pig inoculation from the mesenteric glands was positive for the tubercle bacillus. Some of these cases look streptococcic. Marked leukopenia is important in diagnosis.

CARROLL S. WRIGHT, M.D., *Secretary.*

## NEW YORK DERMATOLOGICAL SOCIETY

*Regular Meeting, March 23, 1926*

A. S. CLARK, M.D., *President*

A CASE FOR DIAGNOSIS: RECURRENT PAPULAR ERUPTION. Presented by DR. MACKEE.

A Chinaman, aged 30, who had been in this country for eight years, four of which had been spent at Saranac Lake for the treatment of pulmonary tuberculosis, exhibited a papular eruption of three months' duration, which occupied all surfaces of the left leg and thigh. The papules were hard, oval, and very dark brown, and they were grouped. None of the lesions showed necrosis, but there were a number of scars due to former lesions. Most of the lesions healed without producing a scar. There were no subjective symptoms. The lesions ranged in size from a pinhead to a split pea.

An examination of the one lesion removed showed granulation tissue only, so that it was impossible to establish a pathologic diagnosis. The patient said that there had been several attacks during the past four years, most of which began with a chill and high fever. The eruption usually lasted about six months. On two occasions, the leg had been badly swollen, and some swelling occurred when the leg was used very much. The Wassermann reaction was negative on several occasions.

DISCUSSION

DR. WHITEHOUSE: I am inclined to consider the eruption a necrotic tuberculid of some type, secondary to the fever. Analogous eruptions are encountered in leprosy after attacks of fever.

DR. WILLIAMS: The man has what is clinically tinea between the toes of both feet, particularly the one affected, and he said to me that at the outbreak there was a good deal of inflammation. In tricophytid, the part most likely to be affected is that near the focus of infection. It is possible that this man had a tinea of the left foot and has enough absorption to cause a tricophytid of this type. Similar cases have been described as erythema nodosum, and in some the nodules ulcerated. That is presented as a possibility. I think that, on the whole, viewing all the evidence, the tubercle bacillus is at the bottom of the condition. In toxic eruptions it is often difficult to determine the offending organism.

DR. MACKEE: The syndrome does not fit any disease with which I am acquainted. The pigmentation, scarring and unilateral distribution and grouping suggest syphilis. The numerous attacks, fever and swelling, are against syphilis. Papulonecrotic tuberculid is always bilateral, and it is not associated with chills and fever and edema; also, the lesions are distinctly necrotic. Chronic recurrent lymphangitis does not produce a papular eruption of this type. It may be necessary to observe and study the patient for a long time before a definite diagnosis will be possible.

A CASE FOR DIAGNOSIS: PAPULONECROTIC TUBERCULID? Presented by DR. BECHET.

A. P., a woman from Dr. Whitehouse's service, aged 27, said that the lesions began three years previously. On the left ankle extending over the dorsal surface of the foot, were innumerable papules which ranged in size

from that of a lentil to that of a split pea. They varied in color from violaceous to brown. The small papules were follicular and flat; the others were elevated and some exhibited necrotic centers. There were a few varioliform scars on the forearms. Some of the lesions on the ankle were characteristic of papulonecrotic tuberculid, yet many others resembled a disseminate miliary lupus vulgaris. The Pirquet reaction was positive.

DISCUSSION

DR. WISE: In my opinion it is lichen scrofulosorum and papulonecrotic tuberculid.

DR. HIGHMAN: I practically agree with Dr. Wise, but cannot agree that it implies any real differentiation between lichen scrofulosorum and those papulonecrotic tuberculids which are tuberculous. I think in this patient different stages of development are shown. If we traced papulonecrotic tuberculids from their start we would find that they begin as small tuberculous lesions—which are tubercles—and that the older and larger lesions are a further development of these, beginning to organize and hence not tuberculous in aspect.

DR. WILLIAMS: I take issue with Dr. Highman. The lesions of lichen scrofulosorum are always superficial, always small, usually very close-set; they never ulcerate, and they do not produce scars; whereas papulonecrotic lesions are deep at first, later involve the epidermis, become necrotic in the center, and disappear leaving a scar. Histologically, they may both be tuberculids, but clinically they are different manifestations and one does not change into the other.

DR. HIGHMAN: There is really no confusion between Dr. Williams' opinion and mine. I did not say that this was lichen scrofulosorum or that it began as lichen scrofulosorum. I said I thought the processes began in the same way and that they were essentially similar—tuberculosis. As regards Dr. Williams' statement that lichen scrofulosorum never ulcerates, I think I recall a picture in Lewandowsky's monograph showing that it does.

DR. WISE: I believe that the large lesions are papulonecrotic tuberculids and the small papules are lichen scrofulosorum. Clinically, the two eruptions do not resemble each other—the first being large, broken-down papule, the second a pinhead-sized, smooth-surfaced papule which does not break down in the center. In this patient, both types of lesions are seen in the same area of skin. Histologically, the papulonecrotic tuberculid usually presents what the German writers are in the habit of calling a "baval" inflammation, the ordinary type of inflammatory reaction. This is found in most of the histologic sections of well developed papules. It is only in the very young papules, especially in those seen in infants, that the true tuberculous structure is encountered in papulonecrotic tuberculid. On the other hand, the histology of lichen scrofulosorum is always that of a tubercle, as it is in lupus vulgaris. Tubercle bacilli are rarely found in lesions of papulonecrotic tuberculid, but in lichen scrofulosorum they are often demonstrated in the lesion.

ANGIOMA AND VERRUCOUS NEVUS. Presented by DR. MACKEE and DR. WISE.

A. B., a boy, aged 18 months, presented an irregular, diffuse and raised purplish-red and verrucous-like lesion on the right leg, thigh and foot. In places the lesion was not elevated, showing distinctly dilated blood vessels; in other areas, it was raised and hyperkeratotic.

A Case for Diagnosis: Pityriasis Rubra Pilaris (?). Presented by Dr. Williams.

C. N., a woman, aged 52, said that the disease began two years previously. The eruption began over the lower part of the sternum, whence a narrow curving band extended under each breast. From the sternum, a broad indefinite band extended to the waist and there spread to the flanks. Other patches of the same type occurred on both axillary folds, the tops of the shoulders, the upper extremities, the popliteal spaces, the inner aspect of the knees, the front of the knees except over the patella, and on the dorsal and lateral aspects of the feet posterior to the toes. The eruption consisted of small, rounded brownish-red papules, generally discrete, but in some places, as over the abdomen, the redness and thickening were confluent, forming irregular patches. There was little scaling except on the elbows and knees. The palms and soles were not thickened. There were no horny plugs on the forearms or over the phalanges. In addition to the eruption, there were many seborrheic keratoses scattered over the trunk. The Wassermann reaction was negative.

Biopsy showed dermatitis, with no suggestion of pityriasis rubra pilaris.

DISCUSSION

Dr. MacKee: I regard the eruption as an eczema, beginning in and around the follicles at which time it resembles the follicular seborrheic dermatitis described by Trimble. Apparently such eruptions may have both external and internal causes. The external cause may be fungi, bacteria or chemicals; the internal causes may be toxic, as a result of intestinal autointoxication, faulty elimination, etc.

Dr. Wise: I agree with Dr. MacKee, especially in regard to the lesions just below the sternum. The whole eruption seems to be an aberrant type of seborrheic eczema.

Dr. Schwartz and Dr. Whitehouse also agreed with Dr. MacKee.

Dr. Highman: Dr. MacKee has covered the ground fully.

Dr. Howard Fox: In general, I agree with Dr. MacKee. If I had to name the disease, seborrheic dermatitis or seborrheic eczema is as near as I could come to it. I think it would be difficult or impossible to discover the cause of this eruption.

Dr. Williams: I think Dr. MacKee suggested a diagnosis of eczema—not seborrheic eczema, not seborrheic dermatitis, just eczema—and I think he is wise. Seborrheic eczema or dermatitis is a very convenient name for certain eruptions on the scalp, face and trunk, characterized by their sharp outline, brownish-red color, and greasy rather adherent scales. They may have nothing to do with the sebaceous glands, but that is another question. They form a fairly distinct clinical entity. Why extend the name to cover an eruption like that shown by this patient, which resembles seborrheic eczema only in its color and, in part, location? Of course, eczema is an indefinite term, used to cover a whole group of dermatoses whose etiology is unknown. As soon as the etiology of any syndrome is established, that dermatosis receives its proper name. Whether at the end there will remain a dermatosis characterized by the recurrent eruption of vesicles singly or in groups and dependent on some metabolic disorder, I do not know, but I think it probable. In the meantime, eczema is a convenient name for dermatitis in which no external etiologic irritant is discovered or probable. The name is a scrap-basket, and for the

present we need a scrap-basket. But why make another scrap-basket by extending the term seborrheic eczema to cover various eruptions whose relationship is at the best very doubtful?

PITYRIASIS RUBRA PILARIS. Presented by DR. HOWARD FOX.

H. N., a married woman, aged 30, born in Hungary, had lived in this country for the past twelve years. The eruption first appeared eighteen months previously and had gradually increased in extent up to the time of presentation. At times there were considerable burning and itching. There was no family history of any skin diseases. Her appendix had been removed seven years before, and a complete hysterectomy had been performed two years later.

Examination showed an extensive generalized eruption of the scalp, face, neck and trunk and extremities. It consisted of diffuse areas of reddish, dry skin, with more or less scaling. Many of the large areas were sharply demarcated, and at their borders were seen a few acuminate papules. According to the patient's description, the eruption had formerly consisted almost entirely of discrete papules, the lesions being "all separate," as she described them. There was a moderate keratotic thickening of the palms and palmar surfaces of the fingers. She was a woman of moderate size, well nourished and in apparent good general health.

DISCUSSION

DR. MACKEE: I should like to know whether Dr. Fox has had any experience with roentgen-ray treatment of these undoubted cases of pityriasis rubra pilaris.

DR. HOWARD FOX: I have not had much experience, but will be glad to treat the patient in this manner. In many of these cases there are remissions without apparent cause. In the well-known case of Bertha Schmidt (appearing in my father's atlas), a complete remission of fourteen years occurred during a continuous residence at the sea shore.

DR. BECHET: A patient of Dr. Levin showed definite hypothyroid symptoms, and thyroid extract proved effective. I reported a case of pityriasis rubra pilaris in a boy suffering from dystrophia adiposa genitalis—a hypopituitary condition—in which the administration of pituitary extract without local treatment markedly improved the eruption. Yet I feel sure that no glandular extract in the absence of definite hypofunction would have any influence on pityriasis rubra pilaris or on any other dermatosis of unknown origin. To administer glandular extracts haphazardly for dermatologic lesions of unknown origin, without any evidence of dysfunction of the ductless glands, is wrong. On the other hand, results from their administration in definite examples of dysfunction are sometimes astonishingly good. A good deal of the opprobium under which endocrinology now suffers is due to this same hit and miss method of administering glandular extract without any knowledge of the surface markings of dysfunction of one or of a group of ductless glands.

SPIEGLER-FENDT SARCOID. Presented by DR. MACKEE and DR. WISE.

The case of Mrs. I. K. had been previously presented before the Dermatological Section of the New York Academy of Medicine, at the February, 1926, meeting, as a case for diagnosis. Epithelioma, hydrocystoma and lymphosarcoma were suggested. A subsequent biopsy showed the Spiegler-Fendt type of sarcoid.

DISCUSSION

DR. WHITEHOUSE: I agree with the diagnosis.

DR. HOWARD FOX: Clinically, I do not think any one would have made the diagnosis shown by the microscope. At a recent meeting, lymphosarcoma was one of the suggestions made, and it seemed a likely one.

DR. HIGHMAN: Sarcoid of Spiegler-Fendt, so far as I know anything about it, is lymphosarcoma. However, it would be impossible to rule out clinically or histologically the remote possibility that this might be mycosis d'emblée or some form of lymphademia—just as the case that Dr. Howard Fox showed several years ago was localized Hodgkin's disease.

TINEA FAVOSA OF THE SCALP. Presented by DR. BECHET.

F. G., a girl, aged 14, from Dr. Whitehouse's service, was born in the United States of Russian parentage. No history of contagion could be elicited; her parents and brothers and sisters had remained free. On the scalp was an area about the size of a five cent piece, showing some scarring, permanent alopecia, a few sulphur yellow scales, which on removal seemed to dip into the follicles, and a "mousy" odor. An examination of the scales showed *Achorion schönleinii*. The case was presented because of its present rarity in New York. About twelve or fifteen years ago cases were more frequently noted in our large clinics, but for the last few years they have been extremely rare.

DISCUSSION

DR. HOWARD FOX: The strongest argument in favor of favus is Dr. Bechet's statement that he observed typical sulphur-colored cups. The pathologist has made a diagnosis of favus from examination of hairs and a culture of only three or four weeks' duration. Examination of hairs alone is often an insufficient basis on which to make a diagnosis of favus. I also feel that too little time has elapsed to make a diagnosis from the culture. It is often hard to differentiate between favus and one of the faviform trichophytons, especially when the cultures are young. Both of these organisms grow slowly.

SCROFULODERMA. Presented by DR. WISE.

A. B., a man, aged 23, presented a palm-sized patch with a border which was serpiginous in outline, rolled, and raised above the niveau of the skin about a quarter of an inch (0.6 cm.). This border was firm to palpation. The lesion extended from the left ear lobe, following the lower part of the cheek on that side, to a point about 3½ inches (7.7 cm.) along the left side of the neck. The central part of the lesion was atrophic, ulcerative, and exuded pus. The lesion was said to have followed swollen glands on that side of the neck, which had received roentgen-ray and ultraviolet treatment. The duration was two years.

DISCUSSION

DR. MACKEE: The lesion is spreading peripherally, the edges are undermined, the center is cicatrizing, and there is considerable edema and exudation. Fungus infection, bromoderma, iododerma and tuberculosis must be considered.

SCLERODERMA EN BANDE: TERTIARY SYPHILIS. Presented by DR. MACKEE and DR. WISE.

M. C., a woman, gave a definite history of syphilis, and on examination presented fixed pupils. The anterior surface of the right leg presented a

glistening, bandlike, indurated lesion of the skin. It was elongated and well defined. Above the knee, the skin was indurated but did not glisten as it did below. It felt leathery to the touch. There was also a similar palm-sized patch on the skin in the central part of the abdomen; here the skin was bound tightly to the underlying tissue. An examination had been made for the presence of arsenic in the blood and urine, but the reports had not yet been received.

DISCUSSION

DR. WILLIAMS: The scleroderma may be due to arsenic. She may have received arsphenamine. Cases of arsenical poisoning may show no arsenic in the urine until after the administration of sodium thiosulphate. I suggest the use of that drug in this case.

DR. CLARK: I was interested in the case, for it gave me the same impression that Dr. Williams expressed. In Dr. Thorne's and my service we have been studying the effect of arsenic in skin diseases, and the therapeutic results of sodium thiosulphite in three pigmented cases have been marked. We have three cases of scleroderma that showed arsenic after the administration of sodium thiosulphite, and all have improved since. I should think this case might be a scleroderma possibly due to arsenic received in the treatment of syphilis, and I suggest that arsenic be searched for in the urine both before and after injections of sodium thiosulphite.

DR. HOWARD FOX: It is well known that pigmentation is a common feature of scleroderma. It is, of course, possible that in some of the cases it may be due to the habit of the average practitioner of giving arsenic promiscuously in all kinds of skin diseases.

NEVUS FLAMMEUS OF EXTENSIVE DISTRIBUTION. Presented by DR. BECHET.

M. D., a girl, aged 16, from Dr. Whitehouse's service, had had since birth a typical "port-wine" nevus, occupying the entire right side of the face and extending to the neck, arms, trunk and legs in large serpiginous areas of a somewhat paler color than on the face. About half of the body surface was occupied by the nevus. The cornea of the right eye was also affected; it was entirely different from the left eye in both color and density. Vision, however, was normal.

ERYTHEMA NODOSUM. Presented by DR. WISE.

Mr. L. G., aged 29, presented a generalized eruption which had been recurrent during the last eighteen months. On the thigh, various portions of the trunk and on the right side of the neck were numerous broken-down ulcers on the sites of pre-existing lesions. These ulcerations resembled those seen in Bazin's disease. The eruption exhibited at the time the patient was presented had a duration of three weeks. At the beginning of each recurrence, the patient always had to go to bed for a few days, because of chills, headache and a fever of 103 F. He also gave a history of the complete disappearance of the nodules without treatment. His tonsils had been removed six weeks previously. The Wassermann blood test and the sugar and urine analyses were negative. The microscopic study of a section confirmed the diagnosis.

DR. HOWARD FOX: The clinical appearance is unusual. As between an erythema nodosum and erythema induratum, I would certainly favor the latter condition. The lesions of erythema nodosum do not break down and ulcerate as does Bazin's disease.

DR. HIGHMAN: The case does not fit into any of the diagnoses suggested, neither does it fit into that of erythema induratum—which would appeal to me as more likely than erythema nodosum, for if we accepted the hypothesis that this is the condition named for Bazin, the lymphodermal lesions might be sarcoid, for the two often go hand in hand. The appearance would not rule out any condition that might be ascribed to tuberculosis. I would regard it rather as a case of tuberculous bacteremia.

DR. WISE: The patient consulted me about two weeks ago, at which time he presented about a dozen walnut-sized lesions on the trunk and lower extremities, and one lesion on the temple. Some of these have disappeared without treatment other than rest in bed, leaving no trace to mark the former sites. A general examination of the patient by his family physician revealed no abnormalities. The broken-down lesions on the lower extremities probably are due to traumatism. The probable clinical diagnosis is erythema nodosum, and the microscopic section tends to confirm this diagnosis.

DR. WILLIAMS: I think that we shall have to revise our whole conception of the various erythemas. Not one of them can be considered a distinct clinical entity; each may be produced by a variety of causes, and many of them may be produced at one time or another by the same cause. We have to consider a bacterial toxemia as the basis of many of these conditions, although it is difficult to say in any given case whether it is a toxemia, a bacteremia or both.

SYPHILITIC INTERSTITIAL GLOSSITIS, LEUKOPLAKIA AND EPITHELIOMA. Presented by DR. MACKEE and DR. WISE.

J. H., aged 60, presented a lesion on the tongue of four years' duration. He had had a genital chancre thirty-five years previously. There was no secondary eruption. He was treated with inunctions of mercury, and tablets for one year. Leukoplakia was first noticed about four years previously. When presented, there was a widespread leukoplakia which is places was verrucous. The entire tongue was thickened. Where there was no leukoplakia, there was smooth atrophy. On the right side of the tip of the tongue was a pea-sized, verrucous tumor. The case was regarded as representing syphilitic interstitial glossitis with smooth atrophy and leukoplakia and a beginning epithelioma.

DISCUSSION

DR. WHITEHOUSE: I think it is on the border line of carcinoma, developing on a leukeratotic base. The soft granulomatous excrescence is not so suggestive as the area in the center of the patch of leukoplakia which has broken down, and there is infiltration at the base.

DR. WILLIAMS: There is beginning ulceration near the middle of the tip of the tongue and a papillomatous mass on the right side near the tip. Both are probably epitheliomatous on a syphilitic base.

DR. CLARK: It is probably an epithelioma of the tongue; the edge is very hard and firm. I also thought that I felt glands in the submaxillary region.

DERMATITIS MEDICAMENTOSA (PHENOLPHTHALEIN). Presented by DR. BECHET.

L. B., aged 30, from Dr. Whitehouse's service, stated that the lesions had been present for three months. He had been taking "phenolax" and "ex-lax" once a week for months. For two weeks previous to presentation he had not been taking phenolphthalein and the lesions had faded considerably, but the

night before, he had chewed some "feenamint" gum, and the lesions had become bright red again, and were much more itchy. On the arms, trunk and legs were typical rounded, sharply circumscribed, elevated, pinkish-red, nonscaly macules, usually noted in this type of drug exanthem.

MULTIPLE CHANCRE. Presented by DR. CLARK.

E. W., aged 19, born in Bavaria, came to the clinic on March 18, with a history of exposure previous to the appearance of the sore (about January 7). He denied any exposure or kissing since that date. The sore appeared on the lip about March 4, and on the penis about March 6. When examined on March 18, he showed a typical primary sore on the upper lip and one on the shaft of the penis, and a marked glandular enlargement in the lymphatic areas draining these lesions. The Wassermann reaction was ++++. A dark-field examination made on the fifth day after injections of arsphenamine and mercury was negative.

The patient had received two injections of arsphenamine, and the lesions and glandular enlargement had been very much modified.

JOHN E. LANE, M.D., Chairman.

# Book Review

ECZEMA AND URTICARIA. By DR. ERWIN PULAY, Vienna, Urban and Schwarzenberg, 1925.

In this monograph of 190 pages, the author presents a critical analysis of our knowledge of eczema and urticaria. In view of the wide divergence of opinion on the comprehension of eczema, and, indeed, on its justification as a clinical entity, Pulay's discussion is rich and interesting. Hebra's conception of the unity of dermatitis and eczema is contrasted with the contrary opinion of the French school. According to Weidenfeld, not every dermatitis is an eczema, but every eczema is a dermatitis. In eczematous subjects the dermatitis is transformed into eczema. In the pathogenesis of eczema the anatomic constitution of the skin is of great importance, and this is in part inborn and in part acquired. Ichthyosis is an example of a congenital predisposing state, and diabetes of an acquired one.

Kreibich divides eczema into dermatitis eczematosa and neurodermitis; for him artificial dermatitis is excluded from the group. The question as to whether there is a specific eczematous diathesis is answered affirmatively by two schools—but in a different manner. The French school, represented by Besnier, Brocq, Darier, and others, believes in a general or constitutional diathesis, to which the name of "arthritism" has been given. The German school, headed by Jadassohn, Weidenfeld, Bloch, Lewandowsky, and others, believes that the predisposition lies in the epidermis. Weidenfeld, through careful experiments with standardized dilutions of croton oil, came to the conclusion that those subject to eczema exhibit a stronger reaction to irritants than normal persons. Furthermore, there is a period of latency between the time of application of the irritant and the development of reaction. This is shorter in acute eczema than in chronic eczema. Bloch found that subjects who have eczema have seven times as sensitive a skin as normal persons. Nevertheless, 5 per cent of normal persons exhibit a hypersusceptibility to eczematogenic irritants. Kreibich believes that a reflex secondary eczema may develop from sensitizing toxic substances formed in a primary focus.

Anaphylaxis plays a large rôle in eczema. An important question is whether this reaction is of humoral or cellular nature; is there a specific hypersusceptibility of the epidermis? Lewandowsky regards eczema as due to an idiosyncrasy in which the epithelium plays the largest rôle. Bloch believes that a functional disturbance of the blood vessel walls is essential. Bruce's experiments are cited to prove the significance of sensory nerve end disturbances in eczema. Bloch and Lewandowsky say the point of attack of the irritant in eczema is the epidermal cells, while Kreibich accuses the sensory nerve endings in the skin. According to the latter, when there is blood vessel wall irritation, a dermatitis eczematosa results, and when there is sensory nerve end irritation, a neurodermatitis.

The author remarks that as eczema is dermatitis plus itch irritation, and without itch irritation no eczema exists, and itching without implication of the nervous system is inconceivable, we must fall back on Kreibich's conception.

Perhaps one may state the situation simply by saying that eczema is an inflammatory reaction of the skin — a blood vessel reaction — brought about through the nerve paths.

Eczema may be of internal or external origin, or both. Many internal causes may operate: Endocrine disturbances, metabolic errors, gastro-intestinal disorders, etc.

Gans' investigations lead him to believe that there is a shifting of calcium deposit in the skin; in eczema it is richer in the epidermis than in the corium, the reverse of normal. The question of sympathetic and vagus irritation on eczema is discussed. Reference is made to Finkelstein's "water retention" as a cause of some infantile eczemas, and the result in an interesting case is given.

The author has done considerable work in blood chemical analyses, and believes uric acid retention to be responsible for certain cases of pruritus and eczema. For these cases, apart from diet, Pulay advises cinchophen and cinchophen compounds or hexophan lithium or atophanyl (Schering) given intravenously as superior to administration by mouth, although the combination treatment is best. Twenty pages are devoted to a discussion of urticaria, and then fifty-seven pages to an admirable chapter on the therapy of eczema.

The monograph shows the author's wide and intelligent grasp of the difficult subjects discussed. The booklet should be in the library of every dermatologist able to read German.

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